# Exercise for acute respiratory infections

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# Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections (Review)

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[Intervention Review]

# Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

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## ABSTRACT

### Background

Acute respiratory infections (ARIs) last for less than 30 days and are the most common acute diseases affecting people worldwide. Exercise has been shown to improve health generally and may be effective in reducing the occurrence, severity and duration of acute respiratory infections.

### Objectives

To evaluate the effectiveness of exercise for altering the occurrence, severity or duration of acute respiratory infections.

### Search methods

We searched CENTRAL (2014, Issue 6), MEDLINE (1948 to July week 1, 2014), EMBASE (2010 to July 2014), CINAHL (1981 to July 2014), LILACS (1982 to July 2014), SPORTDiscus (1985 to July 2014), PEDro (searched on 11 July 2014), OTseeker (searched on 11 July 2014), the WHO International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov (searched on 11 July 2014).

### Selection criteria

Randomised controlled trials (RCTs) and quasi-RCTs of exercise for ARIs in the general population.

### Data collection and analysis

Two review authors independently extracted data from the included trials using a standard form. We contacted trial authors to request missing data. One review author entered data and a second review author checked this. There were sufficient differences in the populations trialled and in the nature of the interventions to use the random-effects model (which makes fewer assumptions than the fixed-effect model) in the analysis.

**Main results**

We included 11 trials involving 904 adults, published between 1990 and 2014. Eight studies were conducted in the USA, and one each in Canada, Spain and Turkey. Sample sizes ranged from 20 to 154 participants aged between 18 and 85 years old. The proportion of female participants varied between 52% and 100%. The duration of follow-up in the studies varied from seven days to 12 months. The exercise type most prescribed for the intervention was aerobic (walking in 70% of the studies, or bicycle riding or treadmill) at least five times a week. Duration was 30 to 45 minutes at moderate intensity. Participants were supervised in 90% of the studies.

For four of the primary outcomes the results did not differ significantly and all were low-quality evidence (number of ARI episodes per person per year, rate ratio 0.91 (95% confidence interval (CI) 0.59 to 1.42); proportion of participants who experienced at least one ARI over the study period, risk ratio 0.76 (95% CI 0.57 to 1.01); severity of ARI symptoms, mean difference (MD) -110 (95% CI -324 to 104); and number of symptom days in the follow-up period, MD -2.1 days (95% CI -4.4 to 0.3)). However, one primary outcome, the number of symptom days per episode of illness, was reduced in those participants who exercised (MD -1.1 day, 95% CI -1.7 to -0.5, moderate-quality evidence).

We found no significant differences for the secondary outcomes (laboratory parameters (blood lymphocytes, salivary secretory immunoglobulin and neutrophils); quality of life outcomes; cost-effectiveness and exercise-related injuries).

There was good adherence to the intervention with no difference between the exercise and non-exercise groups.

We rated the quality of evidence for the primary outcomes as low for most outcomes using the GRADE criteria: allocation concealment was not reported and there was a lack of blinding; in addition, there was imprecision (the CI is very wide because of a small number of participants) and inconsistency, which may be due to differences in study design.

**Authors' conclusions**

We cannot determine whether exercise is effective at altering the occurrence, severity or duration of acute respiratory infections. One analysis of four trials suggests that the number of days of illness per episode of infection might be reduced by exercise. The small size of the studies, risk of bias and heterogeneous populations trialled all contribute to the uncertainty. Larger studies, with less risk of bias from patient selection, blinding of outcomes assessors, reporting of all outcomes measured and with registration of study protocols, are required to settle the question.

## PLAIN LANGUAGE SUMMARY

**Is exercise effective for changing the occurrence, severity or duration of acute respiratory infections?**

**Background**

Exercise has been shown to improve health generally. We undertook this review to test whether exercise is effective at changing the occurrence, severity or duration of acute respiratory infections, i.e. colds and coughs that last less than a month.

**Study characteristics**

A search of the major databases to July 2014 found 11 trials involving 904 participants between the ages of 18 and 85 years old, which tested the effect of exercise on acute respiratory infection symptoms. Exercise was supervised and prescribed at least five times a week, with 30 to 45 minutes of moderate-intensity activities in most studies.

**Key results**

The number of acute respiratory infections per person per year and the severity of these symptoms were similar in the exercising and non-exercising groups. Similarly, the number of people experiencing at least one acute respiratory infection and the number of symptom days in the follow-up period were similar among people who did or did not exercise. One analysis of four trials suggested that the number of days of illness per episode of infection might be reduced by exercise.

**Quality of evidence**

The quality of the trials was poor, which means that there might be benefit or even harm attributable to exercise.

**Conclusion**

We need further studies with fewer potential biases to understand whether exercise is able to reduce the occurrence, severity or duration of acute respiratory infections.

## SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

**Exercise for acute respiratory infections**

**Patient or population:** healthy people
**Settings:** any setting
**Intervention:** bicycle, treadmill or walk

| Outcomes | Illustrative comparative risks* (95% CI) | | Relative effect (95% CI) | No. of participants (studies) | Quality of the evidence (GRADE) | Comments |
|---|---|---|---|---|---|---|
| | Assumed risk | Corresponding risk | | | | |
| | No exercise | Exercise | | | | |
| **Number of ARI episodes per person per year**<br>Self reported<br>Follow-up: adjusted for 1 year | Median risk in study population | | | | | |
| | **2.5** | **2.3 (95% CI 1.5 to 3.6)** | **Rate ratio 0.91** (0.59 to 1.42) | 213<br>(2 studies) | ⊕⊕◯◯<br>**low**[1,3] | |
| **Proportion of people who experienced at least 1 ARI over the study period**<br>Follow-up: 12 to 52 weeks | Median risk in study population | | | | | |
| | **55 per 100** | **42 per 100 (95% CI 31 to 56)** | **RR 0.76**<br>(0.57 to 1.01) | 219<br>(3 studies) | ⊕⊕◯◯<br>**low** [1,3] | This outcome combines a wide range of follow-up periods |
| **Global severity over 8 weeks**<br>Self reported | **mean 358 points** | **mean 110 lower (324 lower to 104 higher)** | | 98<br>(1 study) | ⊕⊕◯◯<br>**low** [1,2] | This scale is an area under the curve (WURSS-24 score by days of illness) |
| **Number of symptom days over 12 weeks** | Median of study population | | | | | |
| | **mean 8.7** | **mean 2.1 lower (4.4 lower to 0.3 higher)** | | 208<br>(3 studies) | ⊕⊕◯◯<br>**low** [1,3] | |

| | | | | | |
|---|---|---|---|---|---|
| **Number of symptom days per episode of ARI (over 12 weeks)** | Median of study population | | | | |
| | **mean 6.7 days** | **mean 1.1 lower (1.7 lower to 0.5 lower)** | | 256 (4 studies) | ⊕⊕⊕○ **moderate** [1] |

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
**CI:** confidence interval; **RR:** risk ratio

GRADE Working Group grades of evidence
**High quality:** Further research is very unlikely to change our confidence in the estimate of effect.
**Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
**Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
**Very low quality:** We are very uncertain about the estimate.

[1]Limitations in the design and implementation. Risk of selection bias and lack of blinding; allocation concealment not reported in the studies.
[2]Imprecision of results. The confidence interval is very wide because of a small number of participants.
[3]Inconsistency of results. Heterogeneity between studies may be due to differences in populations, intensity and duration of the intervention and length of follow-up period.

# BACKGROUND

## Description of the condition

Acute respiratory infections (ARIs) are the most common acute diseases affecting people worldwide (Bellos 2010; Del Mar 2000). They are defined as infections of the respiratory tract that last for less than 30 days (WHO 1990). ARIs have an estimated worldwide annual death rate of 4.25 million people and a total of one to two years in every person's life is spent suffering from ARIs (Del Mar 2000; WHO 2002; WLF 2010). They are one of the most common causes for consultation in primary care (Thomas 2000). ARIs can be caused by viral or bacterial pathogens. Viral ARIs alone cost the USA USD 40 billion annually in direct and indirect costs (Fendrick 2003). There are preventive strategies against ARIs in the community, including stopping smoking, hand washing, avoiding sick contacts, good nutrition and vaccines (Cohen 1993; Jefferson 2011; Roth 2008).

## Description of the intervention

Exercise has been shown to improve health generally. It may be effective at reducing the occurrence, severity and duration of ARIs (Barrett 2012; Chubak 2006; Nieman 2010; Obasi 2012). We define exercise as "a planned and structured program of motor actions to improve or maintain components of physical fitness" (Carpersen 1985). The types of exercise prescribed can vary by mode, dose, setting, the person who delivers the intervention and any accompanying behavioural strategies (i.e. counselling, pamphlets) (Campbell 2007).

## How the intervention might work

People who regularly exercise enjoy improvements in general health and better maximal oxygen uptake ($VO_2$ max), muscular strength, flexibility and body composition (Warburton 2006). A specific effect on ARIs could theoretically include: decreased age-associated immunosenescence; improved innate immune function; mucosal immunity; decreased inflammatory cytokines and stress resistance (Chubak 2006; Engels 2004; Manzaneque 2004; Nieman 2010).

## Why it is important to do this review

Exercise is a low-cost and readily available intervention that most people could implement. We have identified no prior systematic review that evaluates trial evidence about the effectiveness of exercise for altering the occurrence, severity or duration of acute respiratory infections. Observational studies have shown an association between exercise and decreased rates of ARIs (Chubak 2006; Nieman 2010). However, this might be attributable to several biases.

# OBJECTIVES

To evaluate the effectiveness of exercise for altering the occurrence, severity or duration of acute respiratory infections.

# METHODS

## Criteria for considering studies for this review

### Types of studies

Randomised controlled trials (RCTs) and quasi-RCTs of exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections in the general population. We also planned to include trials that used a cross-over or cluster-RCT design.

### Types of participants

Individuals of all ages including people with chronic respiratory conditions. We considered the definition of ARIs used by the trial authors.

### Types of interventions

We included studies that used exercise in at least one group and compared it to non-exercising or no intervention. We documented all reported details of the intervention duration, frequency of sessions and the season of the exercise programme. Comparisons included were:

1. exercise versus sedentary lifestyle;
2. exercise versus usual care;
3. exercise versus non-exercising.

### Types of outcome measures

#### Primary outcomes

1. Number of ARI episodes per person per year.
2. Proportion of participants who experienced at least one ARI over the study period.
3. Severity of ARI symptoms.
4. Number of symptom days in the follow-up period (12 weeks).
5. Number of symptom days per episode of illness.

### Secondary outcomes

1. Laboratory-assessed immune parameters.
2. Quality of life.
3. Cost to the patient.
4. Exercise-related injuries.
5. Adherence to the group intervention.

## Search methods for identification of studies

### Electronic searches

We searched CENTRAL (2014, Issue 6), which contains the Cochrane Acute Respiratory Infections Group's Specialised Register, MEDLINE (1948 to July week 1, 2014), EMBASE (1974 to July 2014), CINAHL (1981 to July 2014), LILACS (1982 to July 2014), SPORTDiscus (1985 to July 2014), PEDro (11 July 2014) and OTseeker (11 July 2014).

We used the search strategy described in Appendix 1 to search MEDLINE and CENTRAL. We combined the MEDLINE search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE (Lefebvre 2011). We adapted the search strategy to search EMBASE (Appendix 2), CINAHL (Appendix 3), LILACS (Appendix 4) and SPORTDiscus (Appendix 5). We did not use any language or publication restrictions.

### Searching other resources

We searched the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) and ClinicalTrials.gov for completed and ongoing studies (11 July 2014). We checked the reference lists of all primary studies and review articles for additional references. We emailed experts in the field about unpublished data that might be included.

## Data collection and analysis

### Selection of studies

Two review authors (AJG, JK) independently assessed all studies resulting from the database searches by screening titles and abstracts. We identified potentially eligible studies for full-text reading. A third review author (TH) resolved any disagreements. We described reasons for including and excluding trials (Higgins 2011a).

### Data extraction and management

Two review authors (AJG, JK) independently extracted data from the included studies using an online form developed for this purpose. Two review authors (AJG, EB) entered the extracted data into RevMan 2014.

### Assessment of risk of bias in included studies

Two review authors (AJG, JK) independently assessed the risk of bias for each included study using the 'Risk of bias' tool published in *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011b). Two review authors (CDM, EB) resolved any disagreements by discussion. We assessed the risk of bias according to the following domains.

1. Random sequence generation (selection bias).
2. Allocation concealment (selection bias).
3. Blinding of participants and personnel (performance bias).
4. Blinding of outcome assessment (detection bias).
5. Incomplete outcome data (attrition bias).
6. Selective reporting (reporting bias).
7. Other bias (other sources of bias related to particular trial design (cross-over and cluster-randomised) or specific circumstances.

We classified the risk of bias as: low risk, high risk or unclear risk of bias (Higgins 2011b).

### Measures of treatment effect

Types of measurements of treatment effect that we used included the following.

1. Dichotomous data: we used risk ratio (RR) for the binary outcomes: proportion of people who experienced at least one ARI over the study period, exercise-related injuries and adherence to the group intervention.
2. Continuous data: the measures were evaluated in numerical quantity. We combined the results using the mean difference (MD) for measures using the same scale for the outcomes: severity of ARI; number of symptom days in the follow-up period (12 weeks); number of symptom days per episode; laboratory parameters - lymphocytes; quality of life; and financial cost to the patient (USD). We also used standardised MD (SMD) where different scales had been used to evaluate the same outcome for laboratory parameters - IgA; laboratory parameters - neutrophils.
3. Rate: we used rate ratio to compare rates between groups for the outcome number of ARI episodes per person/year.

### Unit of analysis issues

We considered the individual the unit of analysis. No cross-over or cluster-RCTs trials met our inclusion criteria.

### Dealing with missing data

We emailed (with one reminder email) the corresponding trial authors to obtain missing data from published papers needed for our analyses. We checked for consistency between the randomised and analysed individuals to verify the intention-to-treat (ITT) analysis in each outcome.

### Assessment of heterogeneity

We assessed heterogeneity between studies using the $I^2$ statistic to describe the percentage of variability in effect. We considered heterogeneity as substantial if the $I^2$ statistic was above 50%.

### Assessment of reporting biases

If we identified mismatches between study protocols and reports, we contacted the trial authors to clarify the information. We had planned to undertake a funnel plot if 10 or more trials were meta-analysed but there were fewer than 10.

### Data synthesis

We were able to perform meta-analyses with some trials that allowed for the combination of data. We used the forest plot graphics produced by RevMan 2014 to illustrate the meta-analyses. Where a combination of data was not possible, we presented a description of individual studies.

We had planned to use a fixed-effect model if heterogeneity was acceptable ($I^2$ statistic < 50%) but we decided that the nature of the studies was so different (both the nature of the interventions and the populations studied), that we needed to a use a random-effects model instead.

For dichotomous data we were able to perform meta-analyses for the outcomes: proportion of people who experienced at least one ARI over the study period and adherence to the group intervention using RR. We performed the meta-analyses using RR.

For continuous data we were able to perform meta-analyses for the outcomes: number of symptom days in the follow-up period (12 weeks); number of symptom days per episode; laboratory parameters - lymphocytes, IgA and neutrophils. We performed the meta-analysis using MD and SMD.

For rate data we were able to perform a meta-analysis for the outcome number of ARI episodes per person/year. We performed the analysis using the log of the rate ratio and standard errors and the generic inverse variance method.

### Subgroup analysis and investigation of heterogeneity

We conducted the only possible subgroup analysis for the outcome adherence to the group intervention. We conducted this analysis to generate a new hypothesis regarding the effect of the length of the intervention on adherence.

1. Length of intervention (short-term: less than six weeks, medium-term: seven to 15 weeks, long-term: more than 16 weeks).

### Sensitivity analysis

We pooled the included studies to verify whether the impact of risk of bias affected the overall treatment effect of exercising. We also explored which studies contributed to heterogeneity.

### 'Summary of findings' table (SoF)

We developed a 'Summary of findings' table using the methods and recommendations described in section 8.5 and section 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* ( Higgins 2011b; Schünemann 2011a; Schünemann 2011b), and using the GRADEpro software (GRADEpro 2008).

The following primary outcomes are presented in the 'Summary of findings' table: number of ARI episodes per person per year; proportion of people who experienced at least one ARI over the study period; severity of ARI; number of symptom days over 12 weeks; number of symptom days per episode (over 12 weeks). We presented all outcomes in the text of the review.

## RESULTS

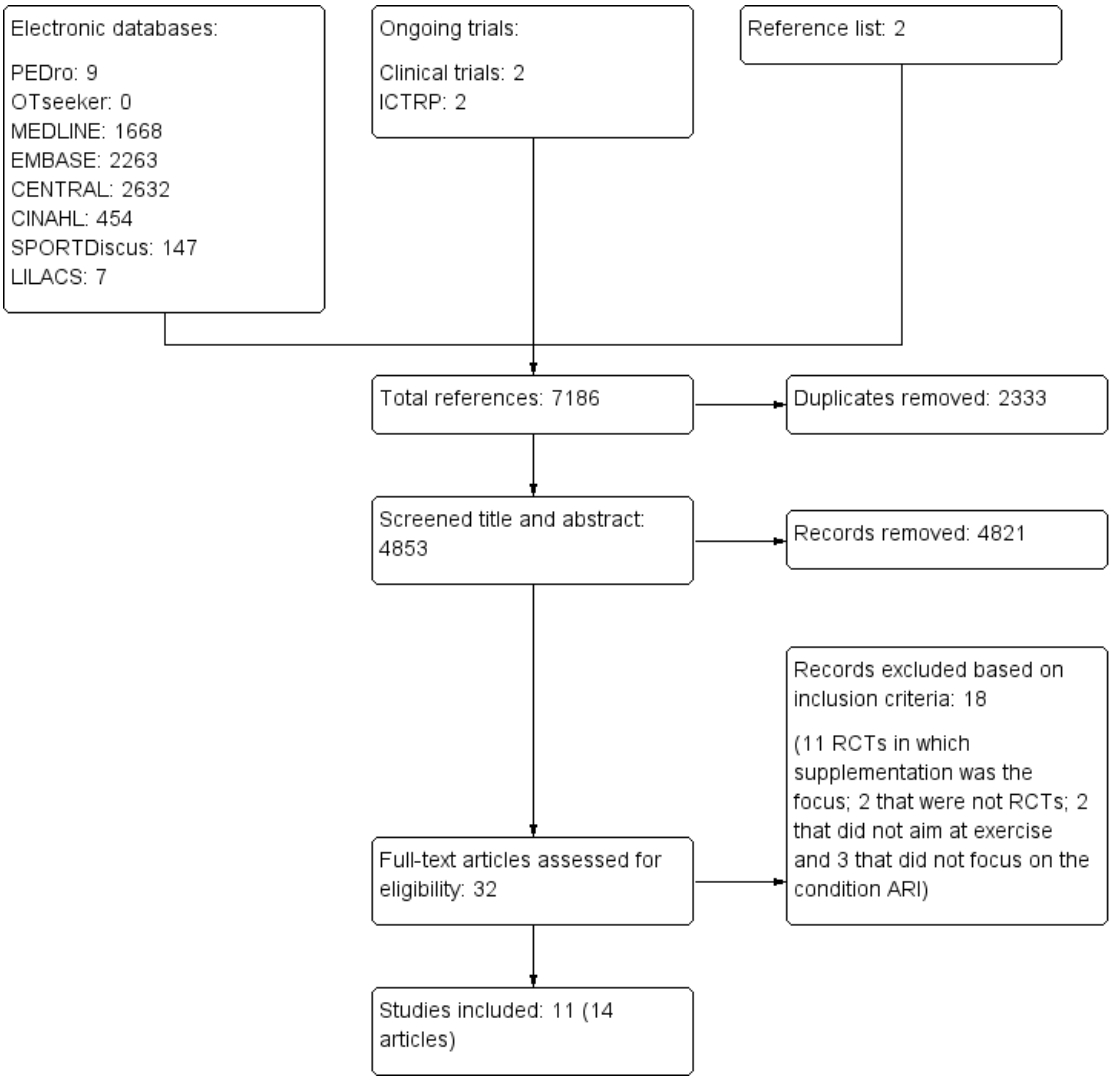
### Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

### Results of the search

See Figure 1.

**Figure 1. Prisma flow diagram.**




We identified 7186 references from the initial search by combining all pre-specified databases, handsearching of reference lists, grey literature and trial register search results. There were a total of 4853 references after duplicates were removed, of which we removed 4821 after title and abstract screening by two review authors. We identified the remaining 32 references as potentially relevant and retrieved full-text articles. From these 32 records, 18 did not meet the inclusion criteria. Two review authors agreed on 14 research papers from 11 trials that fulfilled the study inclusion criteria for this review.

### Included studies

See Characteristics of included studies and Table 1 and Table 2. Eleven trials involving 904 adults, published between 1990 and 2014, met the inclusion criteria. All studies were published in the English language. Eight studies were from the USA (Barrett 2012; Chubak 2006; Nieman 1990; Nieman 1993; Nieman 1997; Sloan 2013; Weidner 1998; Weidner 2003), one was from Canada (Klentrou 2002), one was from Spain (Manzaneque 2004), and one was from Turkey (Cilo˘glu 2005). Sample sizes ranged from 20 to 154 participants. Participants were aged between 18 and 85 years old. The proportion of female participants in each study varied from 52% to 100%. The duration of the exercise interventions varied from seven days to 12 months. The type of exercise

usually prescribed was aerobic, of which bicycle riding, treadmill or walking were prescribed in 73% of the studies. The exercise sessions were performed five times a week (range three to seven times/week) and all trials utilised 30 to 45 minutes of moderate-intensity activities under supervision.

### Excluded studies

We excluded 18 studies, with reasons provided in the Characteristics of excluded studies table.

## Risk of bias in included studies

The risk of bias for each included study is presented in Figure 2 and Figure 3. We found little evidence of selective reporting, although only one study was registered. The main sources of risk of bias were due to poor reporting.

**Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.**

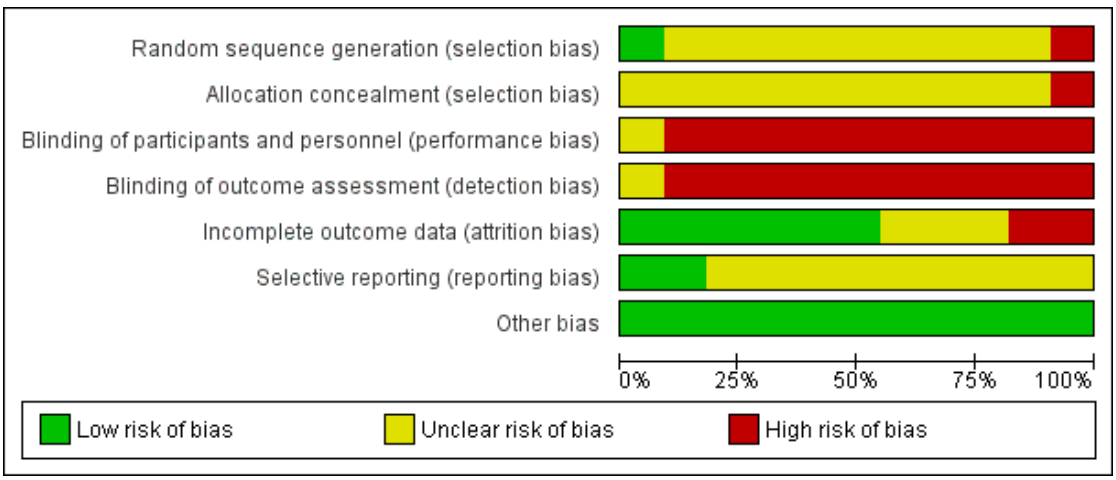
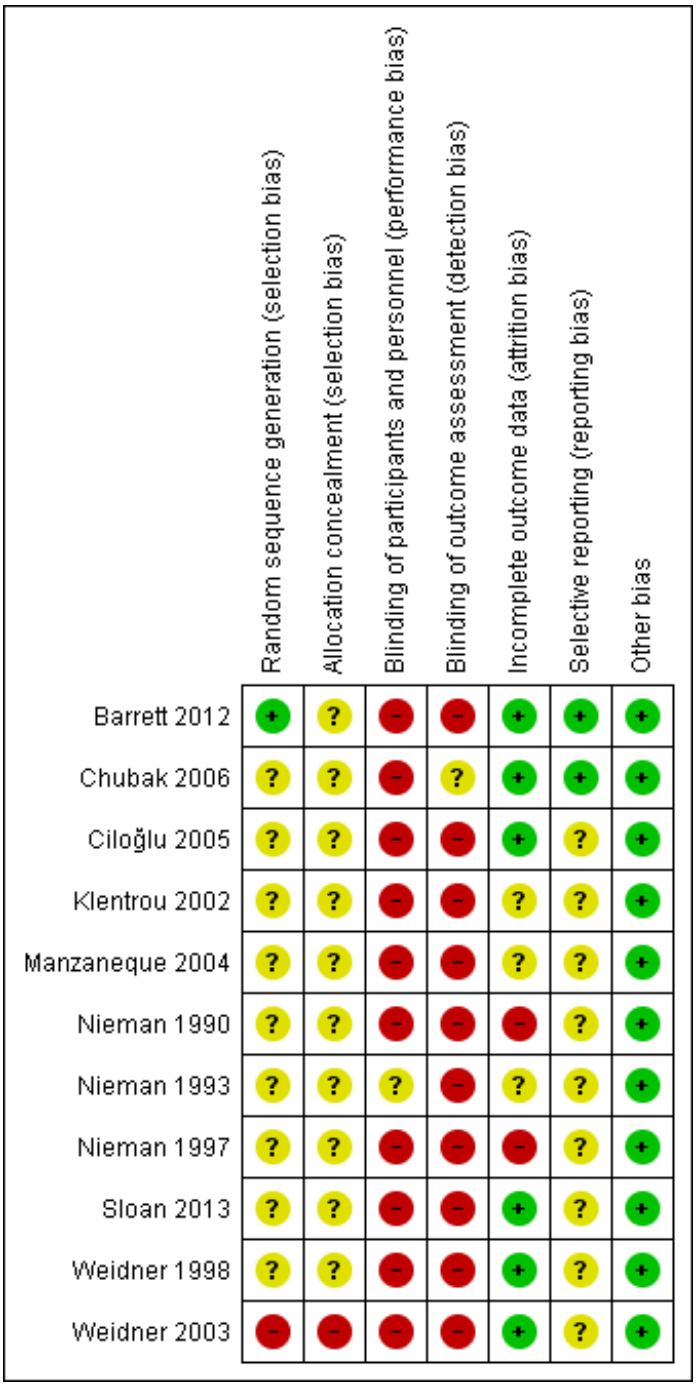


**Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.**



### Allocation

Only one study clearly detailed the randomisation procedure (Barrett 2012), while the other included studies did not provide enough information to allow us to assess this adequately. One study did not randomise adequately (participants were alternately assigned to groups and therefore we judged this as a high risk of bias) (Weidner 2003). We classified allocation concealment as unclear in 90% of studies because of insufficient information in the papers. We judged only one study as high risk of bias because the alternate method of randomisation (making this a quasi-randomised controlled trial) allows prediction of assignment to groups and is therefore easy to manipulate (Weidner 2003).

### Blinding

The nature of the study interventions meant that blinding of participants was not possible and we classified all studies as 'high' risk of bias. Outcome assessor blinding was unclear because every study provided insufficient information, except for Chubak 2006, which collected outcome information by telephone interview and Nieman 1990, who blinded participants to the study objectives.

### Incomplete outcome data

We classified six studies as low risk of bias because they lost few participants to follow-up, or reported missing data on colds or other upper respiratory tract infection and adjusted data analysis. Nieman 1990 and Nieman 1997 reported substantial loss to follow-up and in the statistical analysis no intention-to-treat analysis was used. We judged the other studies as having an unclear risk of bias.

### Selective reporting

Only Barrett 2012 registered the trial prior to conducting the study (therefore was 'low' risk of bias). We judged the other studies as 'unclear' risk of bias because of incomplete reporting rather than any detected differences between methods and results.

### Other potential sources of bias

We judged all included studies to be free from other sources of bias.

## Effects of interventions

See: **Summary of findings for the main comparison** Exercise for acute respiratory infections

### Primary outcomes

#### 1. Number of ARI episodes per person per year

For this outcome we found four relevant trials (n = 213) (Barrett 2012; Chubak 2006; Nieman 1990; Sloan 2013). However, we excluded Nieman 1990 and Sloan 2013 from the meta-analysis due to lack of clarity in the data. Although there was a slightly lower rate in the exercise group, there was no significant difference between exercise and non-exercise for ARI episodes (rate ratio 0.91; 95% CI 0.59 to 1.42, Analysis 1.1). This outcome had moderate levels of heterogeneity ($Chi^2$ test = 2.23; df = 1; P value = 0.14; $I^2$ statistic = 55%). We downgraded the outcome from high to low quality due to limitations in the design and implementation (risk of selection bias and lack of blinding, allocation concealment not reported in the studies) and inconsistency of results (heterogeneity between studies may be due to differences in populations, intensity and duration of the intervention and length of the follow-up period).

#### 2. Proportion of participants who experienced at least one ARI over the study period

For this outcome we found three relevant trials (n = 219) (Barrett 2012; Chubak 2006; Nieman 1993). The difference between participants in the exercise group (who had a lower proportion experiencing acute respiratory infection) and those in the non-exercising group was not statistically significant (risk ratio (RR) 0.76; 95% CI 0.57 to 1.01, Analysis 1.2). This outcome had low levels of heterogeneity ($Chi^2$ test = 2.49; df = 2; P value = 0.29; $I^2$ statistic = 20%). We downgraded the outcome from high to low quality due to limitations in the design and implementation (risk of selection bias and lack of blinding, allocation concealment not reported in the studies).

#### 3. Severity of ARI symptoms

For this outcome we only found one relevant trial (n = 98) (Barrett 2012). There was no significant difference between participants in the exercise group and those in the non-exercise group in the total WURSS-24 score over the duration of episodes of ARI (mean difference (MD) -110.0; 95% CI -323.53 to 103.53, Analysis 1.3). We downgraded the outcome from high to low quality due to limitations in the design and implementation (lack of blinding) and imprecision of results (the confidence interval is very wide because of the small number of participants).

#### 4. Number of symptom days in the follow-up period (12 weeks)

For this outcome we found three relevant trials (n = 208) (Barrett 2012; Klentrou 2002; Nieman 1997). Nieman 1997 had a factorial design: we combined the data for exercise and exercise and diet and compared this combination with the combination of diet alone and control. The exercise group had a mean of two days fewer symptom days, but there was no statistically significant difference between participants in the exercise group and those in the non-exercise group (MD -2.06; CI -4.39 to 0.27, Analysis 1.4). This outcome had moderate levels of heterogeneity ($Chi^2$ test = 3.12; df = 2; P value = 0.211; $I^2$ statistic = 36%). We downgraded the outcome from high to low quality due to limitations in the design and implementation (risk of selection bias and lack of blinding, allocation concealment not reported in the studies) and inconsistency of results (heterogeneity between studies may be due to differences in populations, intensity and duration of the intervention, and length of the follow-up period).

#### 5. Number of symptom days per episode of illness

For this outcome we found four relevant trials (n = 256) (Barrett 2012; Ciloğlu 2005; Nieman 1990; Sloan 2013). There was a statistically significant difference between participants in the exercise group and those in the control group in the number of days per episode of ARI, with the exercise group having approximately one day less with symptoms in each episode (MD -1.13 days; 95% CI -1.71 to -0.54, Analysis 1.5). This outcome had low levels of heterogeneity ($Chi^2$ test = 3.3; df = 3; P value = 0.35; $I^2$ statistic = 9%). We downgraded the outcome from high to moderate quality due to limitations in the design and implementation (risk of selection bias and lack of blinding, allocation concealment not reported in the studies).

### Secondary outcomes

#### 1.1. Laboratory-assessed immune parameters - lymphocytes

For this outcome we found three relevant trials (n = 157) (Nieman 1990; Nieman 1993; Nieman 1997). There was a very small mean increase in the exercise group compared with the non-exercise group, but this difference was not statistically significant (MD 0.11; 95% CI -0.10 to 0.31, Analysis 1.6). This outcome had low levels of heterogeneity ($Chi^2$ statistic = 2.21; df = 2; P value = 0.33; $I^2$ statistic = 10%). We downgraded the outcome from high to moderate quality due to limitations in the design and implementation (lack of blinding).

#### 1.2 Laboratory-assessed immune parameters - IgA

For this outcome we found four relevant trials (n = 166) (Ciloğlu 2005; Klentrou 2002; Manzaneque 2004; Sloan 2013). There was no significant difference between participants in the exercise group and the non-exercise group (standardised MD (SMD) 0.07; 95% CI -0.37 to 0.52, Analysis 1.7). This outcome had moderate levels of heterogeneity ($Chi^2$ test = 5.14; df = 3; P value = 0.16; $I^2$ statistic = 42%). We downgraded the outcome from high to low quality due to limitations in the design and implementation (lack of blinding).

#### 1.3 Laboratory-assessed immune parameters - neutrophils

For this outcome we found three relevant trials (n = 214) (Barrett 2012; Manzaneque 2004; Nieman 1997). There was no significant difference between participants in the exercise group and those in the non-exercise group (SMD -0.11; 95% CI -0.44 to 0.22, Analysis 1.8). This outcome had low levels of heterogeneity ($Chi^2$ test = 2.44; df = 2; P value = 0.3; $I^2$ statistic = 27%). We downgraded the outcome from high to low quality due to limitations in the design and implementation (lack of blinding).

#### 2. Quality of life

Only one study analysed quality of life (n = 98), which was reported in two separate domains (physical and mental health) (Barrett 2012). This study included 47 participants in the exercise group and 51 participants in the control group. The physical health domain (MD 1.40; 95% CI -2.32 to 5.12) and the mental health domain (MD 3.40; 95% CI -0.60 to 7.40) were not statistically significant (Analysis 1.9). We downgraded the outcome from high to low quality due to limitations in the design and implementation (lack of blinding) and imprecision of results (the confidence interval is very wide because of the small number of participants).

#### 3. Cost to the patient (USD)

For this outcome we only found one relevant trial (n = 8) (Barrett 2012). There was no significant difference between participants in the exercise group and those in the non-exercise group (MD -78.00; CI -219.60 to 63.60, Analysis 1.10). We downgraded the outcome from high to low quality due to limitations in the design and implementation (lack of blinding) and imprecision of results (the confidence interval is very wide because of the small number of participants).

#### 4. Exercise-related injuries

For this outcome we only found one relevant trial (n = 30) (Nieman 1993). There was no significant difference between participants in the exercise group and those in the non-exercise group (RR 5.67; CI 0.29 to 108.91, Analysis 1.11). We downgraded the outcome from high to low quality due to limitations in the design and implementation (lack of blinding) and imprecision of results (the confidence interval is very wide because of the small number of participants).

#### 5. Adherence to the group intervention

For this outcome we found eight relevant trials (n = 499) (Barrett 2012; Chubak 2006; Ciloğlu 2005; Klentrou 2002; Manzaneque 2004; Nieman 1990; Nieman 1993; Sloan 2013). There was no significant difference between the participants in the exercise group and those in the non-exercise group (RR 0.98; CI 0.95 to 1.02, Analysis 1.12). This outcome had low levels of heterogeneity (Chi $^2$ test = 6.38; df = 7; P value = 0.50; $I^2$ statistic = 0%). We downgraded the outcome from high to moderate quality due to limitations in the design and implementation (lack of blinding).

### Sensitivity analysis

We found no important levels of heterogeneity for any of the outcomes analysed. Thus, there was no need for further exploration.

## DISCUSSION

### Summary of main results

This review aimed to determine the effectiveness of exercise in altering the occurrence, severity or duration of acute respiratory infections (ARIs). Analysis of the following primary outcomes showed no significant differences between people who exercised and those who did not: number of ARI episodes per person per year; proportion of participants who experienced at least one ARI over the study period; severity of ARI symptoms; and number of symptom days in the follow-up period. However, the primary outcome of number of symptom days per episode was significantly lower in people who exercised. In a subgroup analysis of 'adherence to the intervention group', which we used to consider whether the effect of the length of the intervention affected adherence, we found no significant differences.

Secondary outcomes (laboratory parameters such as lymphocytes, IgA and neutrophils) were similar in both groups. Similarly, for quality of life outcomes we found no significant difference with exercise for physical and mental health quality of life. The one study that presented data on cost-effectiveness found no significant benefits of exercise. The one study that provided data on exercise-related injuries showed no significant difference between people who exercised compared to those who did not. We observed no significant differences in adherence between the exercise or control group.

### Overall completeness and applicability of evidence

Eleven trials randomised 904 participants who commenced the intervention and 35 participants were lost to follow-up. Data were limited in terms of the number of outcomes. Most studies did not provide enough information to enable a secure assessment of risk of bias. We have also highlighted the poor reporting of the studies and most trial authors did not choose patient-centred outcomes.

### Quality of the evidence

Only one study clearly described the randomisation process (Barrett 2012).

The characteristics of exercise interventions mean that it is not possible to blind participants. While outcome assessors could be blinded, only one study provided enough information to confirm this was done.

Attrition bias appeared to be a high risk among some studies. Intention-to-treat analysis, or another statistical strategy, could have been used to adjust for loss to follow-up.

The GRADE quality of evidence for the primary outcomes ranks from high to low across different outcomes, because of the lack of blinding, risk of selection bias (allocation concealment not reported in the studies) and imprecision (the confidence interval was very wide because of the small number of participants).

Several of the studies appear to have focused on pathophysiological processes rather than pragmatic outcomes of interest to patients. This is not a problem of selective reporting so much as a different research objective in these studies compared to the objectives of our review.

### Potential biases in the review process

The main limitation of this review is the lack of information to enable us to appropriately judge the risk of bias, the clinical variability and the lack of consistent criteria for ARI classification. Most trials were not registered, presenting another potential source of bias, although we found no ongoing studies in clinical trials registries.

### Agreements and disagreements with other studies or reviews

We found one narrative systematic review of physical activity and the risk of ARI among athletes. It reported on 30 studies published until 2009 (with 8575 athletes and 1798 non-athletes). The authors highlighted the heterogeneity problem of exercise intensity, duration and the widely variety of participants included in the primary studies, as well as the different types of study designs. The authors were careful to identify the same problems with risk of bias that we did. We are in agreement with the need for better methodological rigour (Moreira 2009). The review also speculates that there is a "J"-shaped curve that describes the relationship between physical activity and risk of ARI (that both low and high levels of physical activity increase the risk of ARI, while moderate levels of

physical activity reduce the risk) (Moreira 2009). Our systematic review could not test this hypothesis because our included studies tested moderate exercise.

Another systematic review using Cochrane methods has evaluated exercise for preventing the common cold and included four randomised controlled trials with a total of 281 participants (Lee 2014). It reports that prevention of the common cold and mean illness days were significantly lower in the exercise groups. One difference between that systematic review and this one appears to be the inclusion criteria: our search was broader and more comprehensive (including more studies and more outcomes).

## AUTHORS' CONCLUSIONS

### Implications for practice

We cannot determine whether exercise is effective at altering the occurrence, severity or duration of acute respiratory infections (ARIs). One analysis of four trials suggests that the number of days of illness per episode of infection might be reduced by exercise. However, this may not be enough to change clinical decision-making (advocating exercise to prevent ARIs) because of the low quality of evidence and the risk of bias in most studies.

### Implications for research

Despite epidemiological data appearing to support a reduced occurrence of ARIs with increased physical activity, more and better randomised controlled trials (RCTs) are needed to answer the question about the effects of exercise on the occurrence, severity and duration of ARIs. Greater methodological rigour is needed for future research (patient selection, blinding of outcome assessors, reporting of all outcomes analysed and registration of study protocols).

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* *Indicates the major publication for the study*

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies *[ordered by study ID]*

**Barrett 2012**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: outpatient clinic adults from University of Wisconsin Department of Family Medicine<br>STUDY PERIOD: 8-week training in mindfulness meditation, matched; 8-week training in moderate-intensity sustained exercise, or observational control. For the analysis we used the exercise group and control group<br>METHODS OF ANALYSIS: "ARI illness episode, severity was assessed once daily using a 24-item version of the Wisconsin Upper Respiratory, Symptom Survey (WURSS). The WURSS-24 adds items assessing headache, body aches and fever to the well-validated WURSS-21. With each ARI illness episode, a nasal wash was collected within 3 days of symptom onset and analysed for interleukin-8 (IL-8), neutrophil count and viral nucleic acid. Elevated neutrophil count and IL-8 levels are indicators of inflammation and correlate with symptom severity and viral shedding. Multiplex polymerase chain reaction (PCR) methods developed and validated at UW were used to identify respiratory viruses. Several validated self report questionnaires were used to explore potential explanatory pathways linking behavioural interventions to ARI outcomes SF-12; PSS-10; Positive and Negative Affect Schedule (PANAS); State Trait Anxiety Inventory (STAI); Life Orientation Test (LOT); Positive Relationships with Others (PR) scale. The Pittsburgh Sleep Quality Index (PSQI); The International Physical Activity Questionnaire (IPAQ); Mindful Attention Awareness Scale (MAAS). Health Care Utilization and Days of Work or School Missed"<br>STATISTICAL ANALYSIS: "the sample size of 150 was based on power estimates contrasting (1) meditation versus control and (2) exercise versus control. To control for multiple testing, a P value $\leq$ 0.025 cutoff for null hypothesis rejection was chosen. 1-sided testing was justified by previously published research, all in the direction of positive results"<br>"Unadjusted between-group contrasts were calculated using 1-sided *t* tests for continuous variables and proportional difference testing for binomials. Most participants did not experience ARI illness, therefore zero inflated regression models were used to control for potential confounders. These models take into account both logistic (incidence) and linear (days of illness or global severity) data. Covariates used in these models were age, sex, education, smoking status, body mass index, baseline physical and mental health (SF-12) and cohort. Global severity was skewed, therefore Box-Cox transformation was used for this outcome in these models. To explore potential causal pathways, we assessed the relationship of secondary outcomes measured just after interventions to the main outcomes" |
| Participants | RECRUITMENT MEANS: community-targeted recruitment methods included advertising in local media<br>TARGET PARTICIPANTS: adults aged 50 years or older<br>N RANDOMISED: 154 adults randomised<br>N COMPLETED: 149 adults completed; 47 (exercise); 51 (meditation); 51 (control)<br>GENDER<br>M = 27; exercise 8, meditation 9, control 10<br>F = 122; exercise 39, meditation 42, control 41 |

| | |
|---|---|
| | AGE: exercise (59.0 ± 6.6), meditation (60.0 ± 6.5), control (58.8 ± 6.8)<br>BASELINE DETAILS: age, gender, smoking, race, BMI, education, income and every questionnaire applied |
| Interventions | SETTING OF INTERVENTION: interventions were conducted at UW Research Park, a multipurpose outpatient clinic with exercise facilities and space suitable for meditation training<br>DESCRIPTION OF INTERVENTION: weekly group sessions were divided into didactic instruction (cognitive, logistic and behavioural) and practice (moderately intensive exercise using stationary bicycles, treadmills and other equipment). For most participants, home exercise consisted of brisk walking or jogging<br>Mindfulness meditation: the standardised 8-week MBSR course includes weekly 2½-hour group sessions and 45 minutes of daily at-home practice<br>Exercise: (8 weeks), contact time (weekly 2½ hour group sessions), home practice (45 minutes per day) and location<br>DELIVERED BY: exercise was applied by 3 qualified exercise instructors in clinical exercise physiology. Meditation was applied by instructors with advanced degrees and all were trained in Massachusetts by the Kabat-Zinn group<br>INTERVENTION PERIOD: 8 weeks<br>FOLLOW-UP PERIOD: 9 months<br>CO-INTERVENTIONS: didactic instruction (cognitive, logistic and behavioural) |
| Outcomes | 1. Physical health, mental health (SF-12)<br>2. Negative emotion (PANAS); positive emotion (PANAS); optimism (LOT); social support (Ryff PR); perceived stress (PSS-10); anxiety (current state) (STAI); sleep quality (PSQI); mindfulness (MAAS)<br>3. Exercise, MET min/wk (IPAQ)<br>4. ARI illness burden: severity and duration (no. days), cold severity, symptoms, based on each ARI illness episode, global severity score (area under the curve, AUC) for all ARI illness days; symptom severity and impact on function and quality of life<br>Data collected (in 2 cohorts) over 7 or 9 months, but reported at 3 months |
| Notes | STUDY FUNDING: "this study was supported by a grant from the National Institutes of Health (NIH), National Center for Complementary and Alternative Medicine (1R01AT004313); and by a grant UL1RR025011 from the Clinical and Translational Science Award (CTSA) Program of the National Center for Research Resources, National Institutes of Health. Aleksandra Zgierska was supported by grant K23 AA017508 from National Institute on Alcohol Abuse and Alcoholism at NIH" |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Low risk | "[ ] software [ ] ... was used to generate 165 unique identification numbers in balanced blocks of 3." |

**Barrett 2012** (*Continued*)

| | | |
|---|---|---|
| Allocation concealment (selection bias) | Unclear risk | "Codes were concealed in consecutively numbered sealed envelopes, which were opened after consent to indicate allocation. " No mention of envelopes being opaque |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcome measurement is by participant self report, therefore cannot be blinded |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | Main outcomes only have data missing for 2 people |
| Selective reporting (reporting bias) | Low risk | The study protocol is available and the pre-specified outcomes were published |
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Chubak 2006**

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|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: Fred Hutchinson Cancer Research Center and the University of Washington<br>STUDY PERIOD: 12 months<br>METHODS OF ANALYSIS: "at baseline and 3, 6, 9 and 12 months, participants completed self administered questionnaires, modified from established, validated instruments on the number of episodes of allergies, upper respiratory tract infections (colds and flu) and other infections over the past 3 months"<br>STATISTICAL ANALYSIS: "Poisson regression allowed for use of data from all available time points without eliminating individuals with some missing data. We assumed an unstructured working correlation matrix, computed robust standard errors and performed an intention-to-treat analysis, with P value < 0.05 being considered statistically significant. Results were identical or stronger when restricted to women who had assessments at all 4 time points. We also evaluated whether the exercise effect differed by age (< 60 versus $\geq$ 60 years) or regular multivitamin use, assessed by abstraction of vitamin bottles brought into the clinic at baseline (see Shade et al for details). All analyses were performed using SAS 8.0 (SAS Institute, Cary, NC) and Stata 8 (StataCorp, College Station, Tex) statistical software. All P values are 2-sided" |
| Participants | RECRUITMENT MEANS: mass mailings and media placements<br>TARGET PARTICIPANTS: post-menopausal women, overweight/obese, non-smoking, sedentary<br>N RANDOMISED: 115 adult post-menopausal women<br>N COMPLETED: 115 post-menopausal women; 53 (exercise) and 62 (control) |

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| | GENDER<br>F = 115; exercise 53, control 62<br>AGE: exercise 60.5 (7), control 60.9 (6.8)<br>Inclusion criteria: "post-menopausal; age, 50 to 75 years; in good health; non-smoking; sedentary (< 60 minutes/week of moderate and vigorous-intensity recreational activity and maximal oxygen consumption < 25.0 mL/kg per minute during a $VO_2$ test); not taking hormone replacement therapy in the past 6 months; alcohol consumption of fewer than 2 drinks per day; body mass index (BMI) between 25 and 40 or BMI 24.0 to 24.9 if body fat > 33%; no history of invasive cancer, diabetes, cardiovascular disease, asthma; no current serious allergies; no regular (≥ 2 times/week) use of aspirin or other nonsteroidal anti-inflammatory medications; not using corticosteroids or other medications known to affect immune function. Women were ineligible if they were volunteering for the study to lose weight, had a history of surgery for weight loss, or were currently attempting, or planning to attempt, weight loss by taking diet pills or entering a structured weight loss programme. Participants had been weight stable for at least 3 months"<br>BASELINE DETAILS: demographic information, medical history, health habits, reproductive history, physical activity, diet and anthropometric variables |
| Interventions | SETTING OF INTERVENTION: Fred Hutchinson Cancer Research Center and the University of Washington<br>DESCRIPTION OF INTERVENTION: "the exercise intervention consisted of at least 45 minutes of moderate-intensity exercise 5 days/week for 12 months. During months 1 through 3, participants were required to attend 3 sessions per week at 1 of the study facilities and to exercise 2 days/week at home. For months 4 through 12, participants were required to attend at least 1 session per week at the facility and to exercise the remaining days on their own for a total of 5 days/week (participants were allowed to exercise additional days at the facility if they chose). The training programme began with a target of 40% of maximal heart rate for 16 minutes per session and gradually increased to 60% to 75% of maximal heart rate for 45 minutes per session by week 8, at which point it was maintained for the duration of the study. Participants wore heart rate monitors (Polar Electro Inc, Woodbury, NY) during their exercise sessions. Facility sessions consisted of treadmill walking and stationary bicycling. Strength training, consisting of 2 sets of 10 repetitions of leg extension, leg curls, leg press, chest press and seated dumbbell row, was recommended but not required to decrease risk of injury and maintain joint stability. A variety of home exercises were suggested and encouraged, including walking, aerobics and bicycling. Participants were encouraged to wear their heart rate monitors when exercising at home. Women randomly assigned to the control group attended weekly 45-minute stretching sessions for 1 year and were asked not to change other exercise habits during the study. Exercise and control participants were asked to maintain their usual diet"<br>DELIVERED BY: not stated<br>FOLLOW-UP PERIOD:12 months<br>CO-INTERVENTIONS: none |
| Outcomes | Multivitamin, number of colds before baseline, number of upper respiratory tract infections, allergy episodes, influenza immunisation<br>PRE-SPECIFIED: 3 months before baseline<br>FOLLOW-UP PERIOD: 12 months |

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| Notes | STUDY FUNDING: "National Cancer Institute (NCI) (R01 CA 69334). Ms. Chubak was supported by grant T32 CA09168 from the NCI. The contents of this publication are solely the responsibility of the authors and do not necessarily represent the official views of the NCI or National Institutes of Health. Dr. Wener was supported in part by the University of Washington Clinical Nutrition Research Grant (DK35816)" |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | "Participants were enrolled in a randomised trial..." Not enough information provided to judge |
| Allocation concealment (selection bias) | Unclear risk | No information regarding allocation concealment was provided in the text |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | Unclear risk | Outcomes are by participant self report. Information was obtained by telephone for outcomes ARI episodes and URI |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | They reported missing data on colds or other upper respiratory tract infection episodes at 6 and 9 months. It was less than 10% |
| Selective reporting (reporting bias) | Low risk | The study protocol is not available, although all relevant outcomes we wanted were reported |
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Ciloğlu 2005**

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| Methods | STUDY DESIGN: parallel-group randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: Genlab Medical Diagnostics and Research Laboratory<br>STUDY PERIOD: September to November<br>METHODS OF ANALYSIS: "the participants had anthropometrical measurements in the fasting state. Body weight and height were measured on standard scale with an attached ruler wearing light clothes and no shoes. Body mass index (BMI) was calculated as weight in kilograms (kg) divided by the square of the height in metres (m). Waist circumference was measured using a flexible measuring tape at the umbilicus level with the participants standing straight, arms at their sides and feet together. Body fat mass and fat free mass were determined by bioelectric impedance. During the supervised sessions, participants were noted for and asked about upper respiratory infection symptoms of runny stuffy nose, sore throat, coughing, sneezing coloured discharge and fever. Those who were in the non-exercise group were phoned weekly for the same data collection. Number of URTI episodes and the number of URTI days per episode were recorded for each participant. An episode of URTI was defined as having the symptoms for more than 2 days and separated by at least 5 days from the previous episode. The saliva samples were collected prior to starting the study and at the end of the 12 weeks each time after the mouth had been rinsed thoroughly with distilled water. The saliva samples were frozen at -20°C and stored until the end of the study period. Salivary IgA concentrations were measured by enzyme linked immunosorbent assay (ELISA) method (Immulon II; Dynex Technologies, Chantilly, Virginia, USA)"<br>STATISTICAL ANALYSIS: not stated |
| Participants | RECRUITMENT MEANS: volunteers from the routine check up from the laboratory<br>TARGET PARTICIPANTS: post-menopausal women<br>N SCREENED: 90 post-menopausal women<br>N COMPLETED: 90 post-menopausal women<br>GENDER<br>F = 90; indoor exercise 30, outdoor exercise 30 and control 30<br>AGE: indoor exercise 55.0 ± 3.5, outdoor exercise 54.6 ± 2.1 and control 30 54.9 ± 3.8<br>EXCLUSION CRITERIA: "excluded for chronic disease, any medications including vitamins, having received the flu shot and having smoked cigarettes within the last 2 years"<br>BASELINE DETAILS: age, weight, BMI, waist circumference, fat mass, fat free mass, number of URTI episodes, number of URTI days per episode |
| Interventions | SETTING OF INTERVENTION: Genlab Medical Diagnostics and Research Laboratory<br>DESCRIPTION OF INTERVENTION: "both the indoor and outdoor exercise groups underwent supervised exercise sessions 5 days a week for 30 minutes each time walking on a treadmill or an outdoor tract respectively at 60% of their maximal heart rate as determined by the simple formula of Maximal Heart Rate = 220 - age. Heart rate measurements were done with a Polar Heart Rate Monitor"<br>DELIVERED BY: supervised sessions<br>FOLLOW-UP PERIOD: 12 weeks<br>CO-INTERVENTIONS: none |
| Outcomes | Salivary IgA levels and the incidence of upper respiratory tract infections<br>FOLLOW-UP PERIOD: 12 weeks |

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| Notes | STUDY FUNDING: not stated | |
| ***Risk of bias*** | | |
| **Bias** | **Authors' judgement** | **Support for judgement** |
| Random sequence generation (selection bias) | Unclear risk | The authors did not explain how the random sequence was generated "They were divided into three groups ... with each group having similar characteristics and randomly assigned." |
| Allocation concealment (selection bias) | Unclear risk | No information regarding allocation concealment was provided in the text |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | There was no loss of data in the outcomes analysed |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Klentrou 2002**

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| Methods | STUDY DESIGN: parallel-group randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: Brock University<br>STUDY PERIOD: February to May 2000<br>METHODS OF ANALYSIS: "to monitor the effectiveness of the exercise programme, both groups were administered a continuous incremental exercise test on an electrically braked cycle ergometer (Ergociser EC-1600, Cateyer Co. Ltd., Japan) for the determination of maximal aerobic power ($VO_2$ max) at 3 separate times during the course of the study: T1 - at the onset of the study (before any activity by the exercise group began) , T2 - at the mid-point of training (6 weeks) and T3 - at the conclusion of training (12 weeks). A volume of 1 ml of unstimulated whole mixed saliva was collected from each participant at T1 and T3 using cylinder-shaped swabs placed in the mouth for 1 minute. Each participant was provided with a Health and Sickness Logbook to record symptoms, as exhibited, daily"<br>"Participants were asked not to take any over-the-counter or prescription medication that might mask their symptoms since the daily sickness log was based on symptoms that the participant experienced or felt"<br>STATISTICAL ANALYSIS: "all statistical analyses were performed using SPSS (SPSS Inc., Chicago Ill.). Comparison of inter-group differences was done using an ANOVA. Changes in maximal [IgAs], [Albs] and [IgAs]:[Albs] with training were analysed using a repeated measurements ANOVA. The accepted level of significance was set at P value < 0.05. The experimental power was more than 99%. Pearson correlation analysis was used to examine the strength of the relationship which existed between URTI and the salivary variables" |
| Participants | RECRUITMENT MEANS: not stated<br>TARGET PARTICIPANTS: healthy men and women<br>N SCREENED: 20 healthy men and women<br>N COMPLETED: 19 completed; 9 (exercise) and 10 (control)<br>GENDER: not informed<br>AGE: 25 to 50 years<br>INCLUSION CRITERIA: "adult men or women (aged 25 to 50 years) having a sedentary lifestyle, non-smokers, free of asthma, no recent influenza immunisation, free from URTI at entry to the study and the women not being pregnant or planning on becoming so. Furthermore, the majority of participants were only indirectly exposed to young children and they all resided in the same area"<br>BASELINE DETAILS: age, $VO_2$ max, IgA |
| Interventions | SETTING OF INTERVENTION: Exercise Assessment and Research Centre<br>DESCRIPTION OF INTERVENTION: "the exercise programme consisted of 3 exercise sessions a week. Each exercise session was 45 minutes long. During the exercise period, the participants performed a 30-minute aerobic protocol at 75% of heart rate reserve using stationary bicycles, treadmills, stair climbers or combined/cross-training using more than 1 device. At the end of the aerobic activities, participants spent an additional 15 minutes doing stretching exercises involving the lower body, trunk and arms. More specifically, each participant performed approximately 10 muscle stretches including: quadriceps, calves, gluteal, lower back, triceps, biceps, shoulder, trapezius and pectoralis. During the aerobic protocol, each participant's heart rate was recorded at 3 different points: prior to starting exercise, mid-point of exercise and completion of exercise (before cool-down) using a Polar heart rate monitor. All exercise sessions were |

**Klentrou 2002** (*Continued*)

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| | conducted in a group format in the Exercise Assessment and Research Center to ensure that participants exercised at the prescribed duration and intensity"<br>DELIVERED BY: not stated<br>FOLLOW-UP PERIOD: 12 weeks<br>CO-INTERVENTIONS: none |
| Outcomes | Influenza symptoms, cold symptoms, total sickness days, $VO_2$ max, symptoms recorded; A concentration ([IgAs]), salivary albumin concentration ([Albs]) and [IgAs]:[Albs]<br>FOLLOW-UP PERIOD: 12 weeks |
| Notes | STUDY FUNDING: Faculty of Health Sciences, Brock University |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors did not explain how the random sequence was generated |
| Allocation concealment (selection bias) | Unclear risk | "After signing the informed consent, participants were randomly assigned to either the control group or the exercise group." Not enough information provided to judge |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | One participant (out of a total of 9) from the exercise group was not included, without reasons given |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Manzaneque 2004**

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| Methods | STUDY DESIGN: parallel group randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: psychology students at the University of Malaga<br>STUDY PERIOD: 1-month training period; Monday to Friday for 30 minutes<br>METHODS OF ANALYSIS: "the day before the study commenced, blood samples were taken from all participants, in both the control and experimental group, at 9:30 in the morning and again 1 month later, at the end of the study, when qigong training was concluded for the experimental participants. The immunological parameters investigated included the number of leukocytes (total leukocytes, monocytes, neutrophils, eosinophils, basophils, lymphocytes, T lymphocytes and T helper lymphocytes), the percentages of leukocytes (monocytes, neutrophils, eosinophils, basophils, lymphocytes and T helper lymphocytes), as well as the concentrations of immunoglobulins (IgA, IgG and IgM) and complement (C3 and C4). Total blood count - Pentra 120 ABX analyser. Serum immunoglobulins and complement Immage, Immunochemistry System (Beckman Coulter)"<br>STATISTICAL ANALYSIS: "a between-group analysis of covariance (ANCOVA) was performed on several dependent variables: the numbers of total leukocytes, monocytes, neutrophils, eosinophils, basophils, lymphocytes, T lymphocytes and T helper lymphocytes; the percentages of lymphocytes, T helper lymphocytes, monocytes, neutrophils, eosinophils and basophils; as well as the concentrations of IgG, IgA, IgM and the complements C3 and C4. The qigong training was considered as an independent variable with 2 levels (absence or control group and presence or experimental group) and the respective pretest scores of each dependent variable as covariants. Thus, the differences between groups were estimated with the differences in pretest scores removed. A P value < 0.05 was considered to be significant, while P value < 0.1 was considered a trend towards significance. Lymphocytes subsets: FACScan (Becton Dickinson)" |
| Participants | RECRUITMENT MEANS: psychology students volunteers<br>TARGET PARTICIPANTS: adults<br>N SCREENED: 29 adults<br>N RANDOMISED: 29 adults randomised<br>N COMPLETED: 26 adults completed; 13 (qigong) and 13 (control)<br>GENDER: M = 12; F = 14<br>AGE: 18 to 21 years old<br>BASELINE DETAILS: age, gender |
| Interventions | SETTING OF INTERVENTION: in a room adjoining the laboratory where the practice sessions were conducted<br>DESCRIPTION OF INTERVENTION: "the form of qigong taught is known as the "eight pieces of brocade" (Ba Duan Jin in Chinese pinyin transliteration). It is a simple qigong method that contains 8 distinct movements and integrates them with breathing and a relaxed state of the mind. The whole physical sequence contains 8 discrete movements each, making a total of 64 physical movements to complete the entire set. Throughout the practice, natural, relaxed and rhythmic breathing is required. This method of qigong reportedly dates back hundreds of years and a number of physical and psychological benefits ts has traditionally been attributed to it. More recently, 2 reports published in important international journals focused on this qigong style and its health-promoting features. 30 minutes per session, 5 days per week for the month-long intervention with instructor. Encouraged to do extra on weekends. No data reported on |

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| | this extra practice"<br>DELIVERED BY: qualified qigong instructor of this discipline<br>INTERVENTION PERIOD: 1 month<br>FOLLOW-UP PERIOD: 1 month<br>CO-INTERVENTIONS: the medication was kept constant during the study period |
| Outcomes | Leucocytes (× 103 cells/$\mu$l and %); monocytes (× 103 cells/$\mu$l and %); neutrophils (× 103 cells/$\mu$l and %); eosinophils (× 103 cells/$\mu$l and %); basophils (× 103 cells/$\mu$l and %); lymphocytes (× 103 cells/$\mu$l and %); T lymphocytes (cells/$\mu$l and %); T helper lymphocytes (cells/$\mu$l and %); IgA (mg/dl); IgG (mg/dl); IgM (mg/dl); C3 (mg/dl); C4 (mg/dl)<br>FOLLOW-UP PERIOD: blood sample at 9:30 in the morning the day before and again 1 month later, at the end of the study |
| Notes | STUDY FUNDING: not stated |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors did not explain how the random sequence was generated |
| Allocation concealment (selection bias) | Unclear risk | "16 subjects were randomly allocated to the experimental group and 13 to the control group, balancing the number of males and females in each case". Not enough information provided to judge |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | "One experimental subject (male) decided to abandon the experiment without reasons given within the first few days of onset and a further two (one male and one female) were excluded from the sample for non-attendance at the qigong sessions on more than two occasions" |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |

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| Other bias | Low risk | The study seems to be free from other sources of bias |

**Nieman 1990**

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| Methods | STUDY DESIGN: parallel-group randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: Loma Linda University<br>STUDY PERIOD: last weekend of January to mid to May 1989<br>METHODS OF ANALYSIS: "all participants reported to the Loma Linda University Human performance Lab for testing at 0700 hours following 12 hours of fasting. After resting for at least 5 minutes, blood samples were collected. Participants returned throughout the day for assessment of the following: height and weight, body composition (hydrostatic weighing and 7-site skinfold tests), resting 12-lead EKG and 12-lead EKG graded exercise testing with metabolic measurements. If a participant exhibited overt symptoms of URI, the appointment was rescheduled. Maximal graded exercise testing was conducted using the Bruce treadmill protocol on the Quinton 44000 stress test system and Q55 treadmill (Quinton Instrument Co., Seattle, WA). Metabolic measurements were taken with the Sensor Medics MMC Horizon System 4400 metabolic cart (Sensor Medics, Anaheim, CA). Log books for daily recording of health problems and exercise patterns were given to each subject at baseline. Heparinised whole blood was used for NK cell number and activity assays and EDTA whole blood for complete blood counts (CBC). CBC were performed on Coulter S-Plus IV instrumentation with visual cell differentials in our clinical hematology laboratory"<br>STATISTICAL ANALYSIS: "results are expressed as mean ± SE. A 2 x 3 repeated measures ANOVA with 1 between-participants factor (EX versus NEX) and 1 within-participant factor (time of testing) was used to analyse the data. When Box's M suggested that the assumptions necessary for the univariate approach were not tenable, the multivariate approach to repeated measures ANOVA was used. In the latter case, Pillais trace statistic was used as the test statistic. With regard to comparison among specific means, only 7 comparisons were of interest to us. These were the contrast of the baseline measures with the $6^{th}$ and $15^{th}$ week measurements within the EX and NEX groups and the contrast between the EX and NEX groups at each of the 3 measurement points. The Dunn-Sidak procedure was used to test these comparisons. Pearson correlations were used to determine the association between change in cardiorespiratory fitness, NK cell activity and URI symptomatology. Comparison between groups for age, BMI and URI were evaluated by simple univariate t-tests" |
| Participants | RECRUITMENT MEANS: not stated<br>TARGET PARTICIPANTS: premenopausal woman<br>N SCREENED: 50 mildly obese premenopausal woman<br>N COMPLETED: 36 completed; 18 (exercise) and 18 (control)<br>GENDER<br>F = 36; placebo 18, probiotic 18<br>AGE: exercise 36.0 (1.6); control 32.8 (1.4)<br>INCLUSION CRITERIA: "25 to 45 years of age, mildly obese (10% to 40% overweight) , premenopausal, 155 cm to 170 cm in height, not presently on an exercise programme or a reducing diet, a non-smoker without a history of alcohol or drug abuse, no current use of medications (except oral contraceptives), absence of hypertension and diabetes |

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| | and no family history of heart disease"<br>BASELINE DETAILS: age, BMI, weight, compliance, NK cell response, metabolic parameters including HR, VE and $VO_2$ |
| Interventions | SETTING OF INTERVENTION: Loma Linda University Human performance Lab<br>DESCRIPTION OF INTERVENTION: for 15 weeks the EX group followed a closely supervised walking programme on a measured course. This consisted of 5 sessions of 45 minute each week at an intensity of 60% of heart rate reserve. To ensure that the participants exercised at a proper intensity, heart rates were monitored by checking pulse rates every 0.8 km. At the completion of 45 min the supervisor recorded their walking distance to the nearest 0.16 km. During the 15-week study, the NEX group was instructed not to participate in any exercise outside of normal daily activity<br>DELIVERED BY: supervised exercises<br>FOLLOW-UP PERIOD:15 weeks<br>CO-INTERVENTIONS: the medication was kept constant during the study period |
| Outcomes | Number of days with ARI; symptoms days per URI; NK cell response, metabolic parameters<br>FOLLOW-UP PERIOD: 15 weeks |
| Notes | STUDY FUNDING: not stated |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors did not explain how the random sequence was generated |
| Allocation concealment (selection bias) | Unclear risk | No description of how allocation was concealed. "Those who qualified for the study were instructed that they would be randomly assigned to an exercise (EX) or non-exercise (NEX) group" |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | Participants were blinded to the study objectives, however more information was needed |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | Substantial loss to follow up: 28% drop-outs, 8 at the beginning of the study and 6 during the study |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |

**Nieman 1990** (*Continued*)

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|---|---|---|
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Nieman 1993**

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| Methods | STUDY DESIGN: parallel-group randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: Appalachian State University<br>STUDY PERIOD: 12 weeks<br>METHODS OF ANALYSIS: "measurement of immune system variables and cardiorespiratory fitness was conducted at baseline in both sedentary and highly conditioned elderly women. Following baseline testing, the 32 sedentary participants were randomly assigned to either the experimental or control group and retested after both 5 and 12 weeks of exercise training. The 5-week testing was conducted to help determine if cardiorespiratory and immune system changes occur early in response to a moderate exercise programme. Maximal oxygen uptake ($VO_2$ max), weight and skin folds at the biceps, triceps, subscapular and supra iliac sites were measured at baseline in highly conditioned and sedentary participants and after 5 and 12 weeks of exercise training. Maximal graded treadmill testing using automated cardiorespiratory monitoring techniques (MMC Horizon System Exercise Evaluation Cart, Sensormedics, Yorba Linda, CA) was performed on all participants using a protocol developed in previous research with elderly participants. Blood specimens were collected from all participants in the seated position at 0700 hours after resting for a minimum of 10 minutes and abstaining from all food, beverages (except water) and vigorous physical activity for at least 12 hours. Samples were taken from the 32 sedentary participants at baseline and then again after 5 and 12 weeks of training. Samples from the 12 highly conditioned elderly participants were taken only at baseline and from the 13 young women only at the 12-week testing. Routine complete blood counts (CBC) were performed using a Coulter STKS instrument (Coulter Electronics, Inc., Hialeah, FL). Heparinised whole blood was used for immune cell phenotyping for analysis of lymphocyte subset profiles"<br>STATISTICAL ANALYSIS: "results are expressed as means ± SE. Baseline comparisons between the elderly and young females were made using simple univariate t-tests. A 2 x 3 repeated measures ANOVA with 1 between-participants factor (walking versus calisthenic groups) and 1 within-subject factor (baseline, 5 and 12 week times for testing) was used to analyse the training data. When Box's M suggested that the assumptions necessary for the univariate approach to repeated measures ANOVA was used. In the latter case Pillais trace statistic was used as the test statistic. With regard to comparison among specific means, only 2 comparisons were of interest to us. These were the contrast of the change in baseline measures with the $5^{th}$ and $12^{th}$ week measurements between the walking and calisthenic groups. The Dunn-Sidak procedure was used to test the comparisons. The chi-square test of association was used to test the relationship between incidence of URTI and varying levels of cardiorespiratory exercise according to group status (highly conditioned, walking and calisthenic groups) during the 12-week study. The Pearson correlation coefficient was used to measure the linear correlationship between immune function and physical fitness (aerobic power and sum of 4 skin-folds) in all elderly women at baseline" |
| Participants | RECRUITMENT MEANS: newspaper advertisements and direct mailings to local senior citizen groups |

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| | TARGET PARTICIPANTS: sedentary healthy elderly women<br>N RANDOMISED: 32 women<br>N COMPLETED: 30 completed; 14 (experimental) and 16 (control)<br>GENDER<br>F = 30<br>AGE: experimental 73.4 (1.1), control 73.5 (1.2)<br>INCLUSION CRITERIA: "between the ages of 67 and 85; did not smoke or abuse alcohol; had not been on a reducing diet or exercise programme (≤ 3 moderate-to-vigorous aerobic sessions of > 20-minute duration per week) for the previous 6 months; were non-diseased (no current symptoms or signs suggestive of heart disease or cancer; did not use medications known to affect immune function)"<br>BASELINE DETAILS: age, sex, height, weight, BMI, Sum of 4 skin-folds, $VO_2$ max |
| Interventions | SETTING OF INTERVENTION: university activity centre<br>DESCRIPTION OF INTERVENTION: "participants in both groups met at the university activity centre and exercised 5 days/week, 30 to 40 minutes per session, under supervision. Participants in the experimental group engaged in 5 sessions of 30-minute to 40-minute brisk walking sessions per week at 60% of their heart rate reserve on either an outdoor or indoor (during bad weather) track. Participants warmed up for 5 minutes before each walking session with range-of-motion callisthenics. Total walking distances were recorded by the supervisor and heart rates monitored every 10 minutes through use of Polar pacer heart rate monitors (Polar USA, Inc.). Walking duration started at 30 minutes and was increased 2 minutes each week until participants were walking for 40 minutes by the mid-point of the study. Training heart rates were recalculated after the 5-week testing to adjust for improvement in cardio-respiratory fitness and ensure that subjects maintained the 60% intensity level. To control for subject expectations and attention, the control group met in the same facility as the experimental group, and engaged in mild flexibility and musculoskeletal calisthenics under the direction of a second supervisor. Emphasis was placed on range-of-motion and stretching movements"<br>DELIVERED BY: supervised exercise<br>FOLLOW-UP PERIOD: 12 weeks<br>CO-INTERVENTIONS: none |
| Outcomes | Leukocyte and lymphocyte subsets; natural killer cell activity; $VO_2$ max; weight, sum of 4 skin-folds; incidence of upper respiratory tract infection<br>FOLLOW-UP PERIOD: 12 weeks |
| Notes | STUDY FUNDING: this research was supported by a grant from the Cybex Corporation through the American College of Sports Medicine Foundation |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors did not explain how the random sequence was generated |

**Nieman 1993** (*Continued*)

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|---|---|---|
| Allocation concealment (selection bias) | Unclear risk | No description of how allocation was concealed; "randomised to either the experimental or control groups" |
| Blinding of participants and personnel (performance bias)<br>All outcomes | Unclear risk | The participants cannot be blinded due to the nature of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Unclear risk | There were 2 participants with missing data |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Nieman 1997**

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|---|---|
| Methods | STUDY DESIGN: factorial randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: Loma Linda University Center<br>STUDY PERIOD: late January to April<br>METHODS OF ANALYSIS: "log books for daily recording of health problems were given to each participant at baseline. Careful verbal and written instructions were given during a pre-study orientation session. Participants recorded health problems each day of the 12-week study using codes used in previous studies. The coded health problems included: 1. No health problems today; 2. Cold symptoms (runny, stuffy nose, sore throat, coughing, sneezing, coloured discharge; 3. Flu symptoms (fever, headache, general aches and pains, fatigue and weakness, chest discomfort, cough); 4. Nausea, vomiting and/or diarrhoea; 5. Muscle, joint or bone problems/injury; 6. Other health problems (describe). The severity of the symptoms was rated by participants as mild, moderate or severe. The number of days with URTI symptoms was calculated for each subject, with days counted only if 2 or more consecutive days of cold or flu symptoms were reported with a mild to severe rating. Body mass and composition were determined for all participants by means of underwater weighing. Residual volume was measured by the nitrogen washout procedure using the System 2100 Computerized Pulmonary Function Laboratory (Sensor Medics Corp, Yorba Linda, Calif). Maximal aerobic power ($Vo_2$ max) was determined using the Bruce graded maximal treadmill protocol (20). Oxygen uptake was measured using the MedGraphics CPX metabolic system (MedGraphics Corporation, St Paul, Minn). Immune assay measurement blood samples were drawn at 7 am from an antecubital vein with participants in the seated position (after 10 to 15 minutes of rest). Routine complete blood counts were performed by clinical haematology laboratory staff using a Coulter STKS instrument (Coulter Electronics, Hialeah, Fla)"<br>STATISTICAL ANALYSIS: "statistical significance was set at the P value < 0.05 level and values are expressed as mean ± standard deviation. Data analysed using a 4 (control, exercise, diet, exercise+diet groups) x 2 (pre- and post-study) repeated measures ANOVA. Duncan multiple comparison test. Pearson product-moment correlations for changes in body mass, body mass index, body fat mass and $VO_2$ max" |
| Participants | RECRUITMENT MEANS: participants were recruited from the surrounding community through advertisements<br>TARGET PARTICIPANTS: obese females<br>N SCREENED: 102 obese females<br>N COMPLETED: 91 completed; 22 (control); 21 (exercise); diet (26); exercise + diet (22)<br>GENDER<br>F = 91<br>AGE: 45.6 ± 1.1<br>INCLUSION CRITERIA: "between the ages of 25 and 75 years; in good health with no known diseases, including diabetes, cancer and heart disease; body mass index (BMI, calculated as $kg/m^2$) between 25 and 65 for obese participants and less than 25 for non-obese participants; not currently following a reducing diet or exercise programme not using medications known to affect immune function; not using supplements in excess of 100% of the Recommended Dietary Allowance on a regular basis; not experiencing chronic pain, marked sleep disturbance, serious allergies, salient emotional or mood problems; no recent history of systemic infection, bone fracture, or surgery; and not smoking cigarettes or abusing alcohol"<br>BASELINE DETAILS: compliance, body composition and immune function, blood cholesterol, triglycerides and glucose |

| | |
|---|---|
| Interventions | SETTING OF INTERVENTION: indoor track<br>DESCRIPTION OF INTERVENTION: participants in 2 exercise groups (E and ED) were required to walk 5 times a week, 45 minutes per session, at 60% to 80% of maximum heart rate (MHR), for 12 weeks (60 total exercise sessions). Supervised sessions were held 4 days per week at an indoor track with duration, heart rate and distance walked measured and recorded. Participants walked 1 session per week without supervision. Duration and intensity of exercise was gradually increased over a 3-week period from 25 to 30 minutes/session at 60% to 65% MHR during the first week to 45 minutes at 70% to 80% MHR from weeks 4 to 12. Participants in the 2 non-walking groups (C and D) reported to the exercise facility 4 days week for a 45-minute session of stretching and mild range-of-motion callisthenic exercises<br>DELIVERED BY: supervised sessions<br>FOLLOW-UP PERIOD: 12 weeks<br>CO-INTERVENTIONS: none |
| Outcomes | Body composition, aerobic power and immune function, blood cholesterol, triglycerides and glucose, days of URTI<br>FOLLOW-UP PERIOD: 12 weeks |
| Notes | STUDY FUNDING: this work was funded by The Cybex Grant from the American College of Sports Medicine |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors did not explain how the random sequence was generated |
| Allocation concealment (selection bias) | Unclear risk | No description of how allocation was concealed. "Before being included in the study, participants had to agree to be randomised to any 1 of the 4 groups (control, exercise, diet, diet and exercise)" |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | High risk | There was loss of 10.8% (drop-outs) and no intention-to-treat analysis was used |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |

| | | |
|---|---|---|
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Sloan 2013**

| | |
|---|---|
| Methods | STUDY DESIGN: prospective randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: information not provided<br>STUDY PERIOD: information not provided<br>METHODS OF ANALYSIS: "each participant visited the exercise physiology laboratory before the first experimental test session for screening purposes and to familiarise themselves with the laboratory testing procedures. At this session, participants also provided written informed consent. During this preliminary visit participants underwent the same test procedures that were used during subsequent graded maximal exercise testing except that the graded exercise test protocol was stopped once a participant reached an exercise intensity level corresponding to 75% of her age-predicted maximal heart rate (HR max = 220 - age) and successfully demonstrated the ability to maintain this level of exercise intensity for 30 minutes without becoming unduly fatigued"<br>Inclusion criteria for participant selection were: "(1) female; (2) 1 to 5 years since cessation of menses; (3) FSH levels > 40 IU/L; (4) not on oestrogen replacement therapy; (5) sedentary, defined as no participation in a regular exercise programme for 2 or more times per week for at least 20 minutes per session or in a participative sport at least twice per week during the preceding 6 months; (6) written clearance from personal primary health care provider to participate in the study; and (7) willingness to accept random assignment"<br>STATISTICAL ANALYSIS: "using a 2 sample t test, the differences in the mean EG and CG at baseline on key demographic variables of age, height, weight, body mass index (BMI), FSH and $VO_2$ max between the 2 groups were evaluated. The distributions of all obtained measures were plotted graphically for visual inspection regarding deviation from normality. The result of the Shapiro-Wilk Test for Normality indicated that the null hypothesis for normality assumptions of mucosal immune measures could not be rejected. The mucosal immune measures data were analysed using multivariate repeated measures analysis of variance (ANOVA). To compare the difference in outcome variables from the baseline and subsequent measurements, the contrast and profile transformations in repeated-measures ANOVA were employed. A P value of < 0.05 was considered statistically significant. For simultaneous testing of hypotheses, the Bonferroni method for controlling the overall error rate was used. All statistical analysis was performed using Statistical Analysis System (SAS, version 9.2) software. Values have been shown as means ± standard deviations" |
| Participants | RECRUITMENT MEANS: information not provided<br>TARGET PARTICIPANTS: healthy post-menopausal women<br>N SCREENED: 32 participants<br>N COMPLETED: 32 participants<br>GENDER<br>F = 32; intervention 16, control 16<br>AGE: 54.1 ± 5.3 years old<br>BASELINE DETAILS: age, gender, physical activity profile, symptom checklist, health history, immune deficiency, medications |

**Sloan 2013** (*Continued*)

| | |
|---|---|
| Interventions | SETTING OF INTERVENTION: home-based walking programme<br>DESCRIPTION OF INTERVENTION: 5 days/week of 30-minute brisk walking at a prescribed moderate aerobic exercise intensity corresponding to 75% of individual HRmax<br>DELIVERED BY: self delivered<br>INTERVENTION PERIOD: 16 weeks<br>CO-INTERVENTIONS: none described |
| Outcomes | Height, weight, BMI, FSH, VO2max, VE max, RER max, HR max, SIgA measures, incidence and duration of URTI<br>FOLLOW-UP PERIOD: 16 weeks |
| Notes | STUDY FUNDING: Supported by NIH/NINR R01 NR 008024 |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors mention randomisation, but they do not describe it |
| Allocation concealment (selection bias) | Unclear risk | The authors do not describe how participants were allocated. "Following random assignment to the EG or CG ..." |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | There was no loss to follow-up |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Weidner 1998**

| | |
|---|---|
| Methods | STUDY DESIGN: randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: School of Physical Education at Ball State University<br>STUDY PERIOD: 6 exercise sessions in a 10-day period<br>METHODS OF ANALYSIS: "all participants reported to the laboratory every 12 hours for 10 consecutive days. Beginning on day 2 (the day of the second inoculation), all participants completed a 13-item symptom severity checklist for each reporting period for virus detection and quantification. Just before HRV 16 inoculation, a pre-inoculation nasal wash was taken from all participants. This nasopharyngeal sample, designed to detect most subclinical or incubating respiratory viruses, allowed us to eliminate previously infected participants from the experiment. The cultures were examined by microscope approximately every other day; other standard techniques were used for detection and identification of viruses (e.g. hemadsorption for myxo and paramyxoviruses, acid lability for rhinoviruses, etc.). These cell cultures could not detect all possible viruses (e.g. most coronavirus infections and many coxsackie A viruses). Beginning the day after inoculation (day 2), nasal washings were obtained and virus specimens were quantitated for HRV 16. Instruments included cycling on either the Air-Dyne bicycle (Schwinn Bicycle Co., Chicago, IL) or Cybex MET 100 cycle (Cybex Metabolic Systems, Ronkonkoma, NY); walking or jogging on a treadmill (Trotter, Millis, MA) or at an indoor track; or stair climbing on the Stepmill (Stair Master Sports and Medical Products, Kirkland, WA) . All participants performed the same mode for each training session. HR was monitored continuously via Polar HR telemetry units; rating of perceived exertion via the Borg 6-20 RPE scale was recorded twice per training session"<br>STATISTICAL ANALYSIS: "symptom severity scores from the cold symptom checklist were summed. 3 statistical analysis were performed. A 2 group by 9 measure (2 × 9) repeated measures ANOVA procedure was used to compare the symptom questionnaire mean z-value scores and the mucous weights for days 2 to 10. A participant's values obtained during the a.m. and p.m. testing were averaged to arrive at a participant's value for a day. The statistical power for comparing the differences between the EX and NEX groups over the 9 days (P value < 0.05) was 0.96 for Cohen's medium-sized effect (Eta = 0.25) and 0.99 for his large effect (Eta = 0.37). Preliminary analyses of the questionnaire and mucous data suggested an alternative to the usual ANOVA procedure was desirable. The alternative procedure employed for these data was the assignment of ranks to the data values, normalising the ranks (obtaining normal distribution z-values for percentiles of the ranks) and evaluating the data via conventional ANOVA procedures and F-tests. The other 2 statistical procedures were a 2 by 5 (2 × 5) repeated measures ANOVA for differences between the EX pre- and post-exercise cold symptom scores and a one-way ANOVA for differences between the quantity of recreational physical activity performed by the EX and NEX groups. The statistical power for the EX group pre post differences (P value < 0.05) was 0.67 for Cohen's medium-sized effect (Eta = 0.25) and 0.97 for his large effect (Eta = 0.37). The SPSS MANOVA program (SPSS, Inc., Chicago, IL) was used for these analyses" |
| Participants | RECRUITMENT MEANS: student volunteers solicited from classes<br>TARGET PARTICIPANTS: healthy adults<br>N SCREENED: 50 adult students<br>N RANDOMISED: 50 adults randomised<br>N COMPLETED: 50 adults completed the study; 34 (intervention group) and 16 (control group)<br>GENDER |

**Weidner 1998** (*Continued*)

| | |
|---|---|
| | M = 24; intervention 17, control 7<br>F = 14; intervention 17, control 9<br>AGE: 19 to 29 years old<br>BASELINE DETAILS: age, gender, physical activity profile, symptom checklist, health history, immune deficiency, medications |
| Interventions | SETTING OF INTERVENTION: Ball State University, School of Physical Education laboratory<br>DESCRIPTION OF INTERVENTION: "2 standardised incremental treadmill protocols, 1 for men and 1 for women, were used in this study. Both protocols consisted of 1-minute stages (1-MET increments) and began with 5 to 6 minutes of graded walking and then progressed to running speeds. All participants were encouraged to give a maximal effort and were provided with strong verbal prompts throughout the testing sessions. HR and RPE were recorded during the last 10 seconds of each stage. Exercise training. Within 18 hours of the first inoculation, EX participants began the supervised exercise training programme previously described. Participants were scheduled for 1 of 2 possible exercise times, either morning or evening. Participants who were assigned to exercise in the morning were expected to exercise at the same time for the entire 6 days of training; likewise, participants assigned to exercise in the evening did so regularly. Exercise consisted of training at 70% of HR reserve for 40 minutes, with the mode of exercise designed to match each participant's regular form of workout. Choices included cycling on either the Air-Dyne bicycle (Schwinn Bicycle Co., Chicago, IL) or Cybex MET 100 cycle (Cybex Metabolic Systems, Ronkonkoma, NY); walking or jogging on a treadmill (Trotter, Millis, MA) or at an indoor track; or stair climbing on the Stepmill (StairMaster Sports and Medical Products, Kirkland, WA). All participants performed the same mode for each training session. HR was monitored continuously via Polar HR telemetry units; rating of perceived exertion via the Borg 6-20 RPE scale was recorded twice per training session"<br>DELIVERED BY: supervised by the researchers<br>INTERVENTION PERIOD: 10 days<br>CO-INTERVENTIONS: rhinovirus induced disease |
| Outcomes | Cold symptom, upper respiratory infection and severity of disease measured by questionnaire and facial tissues<br>FOLLOW-UP PERIOD: 10 days |
| Notes | STUDY FUNDING: this research was supported by NIH HL 50123 |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | Unclear risk | The authors did not explain how the random sequence was generated |
| Allocation concealment (selection bias) | Unclear risk | No description of how allocation was concealed. "Fifty subjects who tested negative to the HRV 16 antibody were randomly assigned to the exercise (EX) group or the |

**Weidner 1998** (*Continued*)

| | | |
|---|---|---|
| | | non-exercise (NEX) group" |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | There was no loss to follow-up |
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |
| Other bias | Low risk | The study seems to be free from other sources of bias |

**Weidner 2003**

| | |
|---|---|
| Methods | STUDY DESIGN: quasi-randomised controlled trial<br>LOCATION, NUMBER OF CENTRES: School of Physical Education at Ball State University<br>STUDY PERIOD: 7 days<br>METHODS OF ANALYSIS: "volunteers were interviewed about their physical activity levels and completed a 13-item symptom severity checklist as part of the initial screening process. A physical examination by a doctor and screening included a health history questionnaire about acute and chronic diseases, asthma, bronchitis, chronic colds, allergies, pregnancy, immune deficiency, medications, smoking and physical activity level. Volunteers were sedentary (2 or fewer days a week of recreational exercise for less than 30 minutes a day for the preceding 3 months). Participants had no symptoms of lower respiratory tract illness, were afebrile (< 100°F) and apparently healthy according to the criteria of the American College of Sports Medicine. All participants agreed to refrain from self treating their colds with over the counter medicines. Each participant signed an informed consent form approved by the institutional review board. Participants who completed the study received some remuneration. All participants reported to the laboratory every 12 hours (0700 and 1900) for 7 consecutive days, beginning on the evening of the day on which they were selected into the study. All completed the 13-item symptom severity checklist at each reporting period. They all also completed an activity log during each evening reporting period to monitor their physical activity levels. After the seventh day of the study, participants reported to the laboratory once a day until they were asymptomatic"<br>STATISTICAL ANALYSIS: "symptom severity scores from the cold symptom checklist were summed. 2 statistical analyses were performed. A 2 group (EX and NEX) by 2 factor repeated measures analysis of variance was used to compare the mean symptom questionnaire values of study participants for mornings and evenings (AM/PM) of 6 time periods (DAY) after collection of the baseline symptom data (2 x 2 x 6). The analyses included data obtained for only days 2 to 7 of the study because some study participants were unable to participate on the first day after collection of the baseline data. An independent groups t test was used to compare the number of days from baseline until the study participants were symptom free. The analysis of variance was performed on scores obtained by: (a) subtracting baseline symptom values from values obtained during the study; (b) ranking the resulting difference values; and (c) obtaining normalised z scores for the ranks. A set of polynomial contrasts was specified in the SPSS MANOVA program (SPSS, Inc, Chicago, Illinois, USA) for the day factor. Statistical tests were conducted for the linear relation component of elapsed time from baseline scores and for the relations of the other components combined with the scores. The latter statistical test identified if systematic variation among the score means existed beyond that identified by the linear component - that is, deviation from linearity. The statistical power for evaluating the relation of the day factor with the scores and for the difference between the EX and NEX groups over the days (P value < 0.05) was 0.89 for Cohen's large effect size and 0.45 for his medium effect size (x). A 1 way analysis of variance for differences between the measures on the physical activity logs for the EX and NEX groups was also completed. A P value < 0.05 was considered significant in this investigation" |
| Participants | RECRUITMENT MEANS: newspaper advertisements<br>TARGET PARTICIPANTS: students that acquired a URTI within the preceding 3 to 4 days (typical peak of illness)<br>N RANDOMISED: 22 adult students<br>N COMPLETED: 22 adults completed the study; 11 (intervention group) and 11 |

| | |
|---|---|
| | (control group)<br>GENDER<br>M = 7; intervention 4, control 3<br>F = 15; intervention 7, control 8<br>AGE: ages 19 to 29 years old<br>BASELINE DETAILS: age, gender, physical activity profile, symptom checklist, health history, immune deficiency, medications |
| Interventions | SETTING OF INTERVENTION: Ball State University, School of Physical Education laboratory<br>DESCRIPTION OF INTERVENTION: "by the second day of the study, participants in the EX group began the supervised exercise training sessions. They were scheduled for either a morning or an evening exercise session and were expected to exercise at the same time for all 5 days of the study. Exercise sessions lasted 30 minutes at 70% of target heart rate with the mode of exercise chosen by the participant from the following list of choices: the Air-Dyne bicycle (Schwinn Bicycle Co, Chicago, Illinois, USA); the Cybex MET 100 cycle (Cybex Metabolic Systems, Ronkonkoma, New York, USA); walking or jogging on a treadmill (Trotter, Millis, Massachusetts) or on an indoor track; or stair climbing on the Stepmill (StairMaster Sports and Medical Products, Kirkland, Washington, USA). All participants performed the same mode for each training session. Heart rate was monitored continuously via Polar heart rate telemetry units"<br>DELIVERED BY: supervised by the researchers<br>INTERVENTION PERIOD: 7 days<br>CO-INTERVENTIONS: none |
| Outcomes | Symptom severity/duration<br>FOLLOW-UP PERIOD: until the end of symptoms |
| Notes | STUDY FUNDING: not stated |

***Risk of bias***

| **Bias** | **Authors' judgement** | **Support for judgement** |
|---|---|---|
| Random sequence generation (selection bias) | High risk | The participants were alternately assigned to either group |
| Allocation concealment (selection bias) | High risk | The allocation to group was predictable |
| Blinding of participants and personnel (performance bias)<br>All outcomes | High risk | The participants cannot be blinded due to the characteristics of the intervention |
| Blinding of outcome assessment (detection bias)<br>All outcomes | High risk | Outcomes measured by participant self report |
| Incomplete outcome data (attrition bias)<br>All outcomes | Low risk | There was no loss to follow-up |

| | | |
|---|---|---|
| Selective reporting (reporting bias) | Unclear risk | The study protocol is not available, so we do not have enough information to judge |
| Other bias | Low risk | The study seems to be free from other sources of bias |

°F: Fahrenheit
Albs: salivary albumin
ANCOVA: analysis of covariance
ANOVA: analysis of variance
ARI: acute respiratory infection
BMI: body mass index
C3: complement 3
C4: complement 4
CBC: complete blood counts
CG: control group
CTSA: Clinical and Translational Science Award
EG: exercise group
EKG: electrocardiogram
ELISA: enzyme linked immunosorbent assay
Eta: eta-squared values from multifactor ANOVA
EX: exercise
FSH: follicle-stimulating hormone
HR: heart rate
IgA: immunoglobulin A
IgG: immunoglobulin G
IgM: immunoglobulin M
IL-8: interleukin-8
IPAQ: International Physical Activity Questionnaire
LOT: Life Orientation Test
MAAS: Mindful Attention Awareness Scale
MBSR: mindfulness-based stress reduction
MET: Metabolic Equivalent of Task
NEX: non-exercise
NIH: National Institutes of Health
NK: natural killer
PANAS: positive and negative affect schedule
PR: positive relationships
PSQI: Pittsburgh Sleep Quality Index
PSS-10: perceived stress scale
RER: respiratory exchange ratio
SD: standard deviation
SE: standard error
SF-12: short form 12
SIgA: salivary immunoglobulin A
SPSS: statistical package for the social sciences
STAI: State Trait Anxiety Inventory
URI: upper respiratory infection

URTI: upper respiratory tract infection
VE: pulmonary ventilation
$VO_{2:}$ oxygen uptake

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Bergendiova 2011 | RCT focusing on supplementation and not exercise |
| Biondo 2010 | RCT focusing on supplementation and not exercise |
| Constantini 2011 | RCT focusing on supplementation and not exercise |
| Cox 2007 | RCT focusing on supplementation and not exercise |
| Cox 2010 | RCT focusing on supplementation and not exercise |
| Henson 2008 | RCT focusing on supplementation and not exercise |
| Kekkonen 2007 | RCT focusing on supplementation and not exercise |
| Meyer 2004 | The focus of the intervention was regeneration regimens and not exercise |
| Nieman 2002 | RCT focusing on supplementation and not exercise |
| Peters 1993 | RCT focusing on supplementation and not exercise |
| Rall 1996 | This study did not analyse the condition acute respiratory infection |
| Shing 2007 | RCT focusing on supplementation and not exercise |
| Spence 1990 | This study did not analyse the condition acute respiratory infection |
| Tiollier 2005 | This study did not analyse the condition acute respiratory infection |
| Weidner 1997 | The participants were inoculated with HRV 16 |
| West 2011 | RCT focusing on supplementation and not exercise |
| Yang 2007 | This is not a randomised controlled trial |
| Yang 2008 | This is not a randomised controlled trial |

RCT: randomised controlled trial
HRV: human rhinovirus type 16

## DATA AND ANALYSES

**Comparison 1. Exercise versus control intervention for acute respiratory infections (total)**

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Number of ARI episodes per person/year | 2 | 213 | Rate Ratio (Random, 95% CI) | 0.91 [0.59, 1.42] |
| 2 Proportion of people who experienced at least one ARI over study period | 3 | 219 | Risk Ratio (M-H, Random, 95% CI) | 0.76 [0.57, 1.01] |
| 3 Severity of ARI | 1 | 98 | Mean Difference (IV, Random, 95% CI) | -110.0 [-323.53, 103.53] |
| 4 Number of symptom days in the follow-up period (12 weeks) | 3 | 208 | Mean Difference (IV, Random, 95% CI) | -2.06 [-4.39, 0.27] |
| 5 Number of symptom days per episode | 4 | 256 | Mean Difference (IV, Random, 95% CI) | -1.13 [-1.71, -0.54] |
| 6 Laboratory parameters - lymphocytes | 3 | 157 | Mean Difference (IV, Random, 95% CI) | 0.11 [-0.10, 0.31] |
| 7 Laboratory parameters - IgA | 4 | 166 | Std. Mean Difference (IV, Random, 95% CI) | 0.07 [-0.37, 0.52] |
| 8 Laboratory parameters - neutrophils | 3 | 214 | Std. Mean Difference (IV, Random, 95% CI) | -0.11 [-0.44, 0.22] |
| 9 Quality of life | 1 | | Mean Difference (IV, Random, 95% CI) | Totals not selected |
| 9.1 Physical health | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 9.2 Mental health | 1 | | Mean Difference (IV, Random, 95% CI) | 0.0 [0.0, 0.0] |
| 10 Cost to the patient (USD) | 1 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 11 Exercise-related injuries | 1 | | Risk Ratio (M-H, Random, 95% CI) | Subtotals only |
| 12 Adherence to the group intervention | 8 | 499 | Risk Ratio (M-H, Random, 95% CI) | 0.98 [0.95, 1.02] |

## Analysis 1.1. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 1 Number of ARI episodes per person/year.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

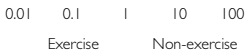
Outcome: 1 Number of ARI episodes per person/year

| Study or subgroup | Exercise N | non-exercise N | log [Rate Ratio] (SE) | Rate Ratio IV,Random,95% CI | Weight | Rate Ratio IV,Random,95% CI |
|---|---|---|---|---|---|---|
| Barrett 2012 | 47 | 51 | -0.3524 (0.25) | | 41.9 % | 0.70 [ 0.43, 1.15 ] |
| Chubak 2006 | 53 | 62 | 0.100388 (0.17157) | | 58.1 % | 1.11 [ 0.79, 1.55 ] |
| **Total (95% CI)** | **100** | **113** | | | **100.0 %** | **0.91 [ 0.59, 1.42 ]** |

Heterogeneity: Tau² = 0.06; Chi² = 2.23, df = 1 (P = 0.14); I² =55%

Test for overall effect: Z = 0.40 (P = 0.69)

Test for subgroup differences: Not applicable




## Analysis 1.2. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 2 Proportion of people who experienced at least one ARI over study period.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 2 Proportion of people who experienced at least one ARI over study period

| Study or subgroup | Exercise n/N | Non-exercise n/N | Risk Ratio M-H,Random,95% CI | Weight | Risk Ratio M-H,Random,95% CI |
|---|---|---|---|---|---|
| Barrett 2012 | 17/47 | 28/51 | | 30.3 % | 0.66 [ 0.42, 1.04 ] |
| Chubak 2006 | 28/42 | 38/49 | | 63.5 % | 0.86 [ 0.66, 1.12 ] |
| Nieman 1993 | 3/14 | 8/16 | | 6.1 % | 0.43 [ 0.14, 1.31 ] |
| **Total (95% CI)** | **103** | **116** | | **100.0 %** | **0.76 [ 0.57, 1.01 ]** |

Total events: 48 (Exercise), 74 (Non-exercise)

Heterogeneity: Tau² = 0.01; Chi² = 2.49, df = 2 (P = 0.29); I² =20%

Test for overall effect: Z = 1.90 (P = 0.057)

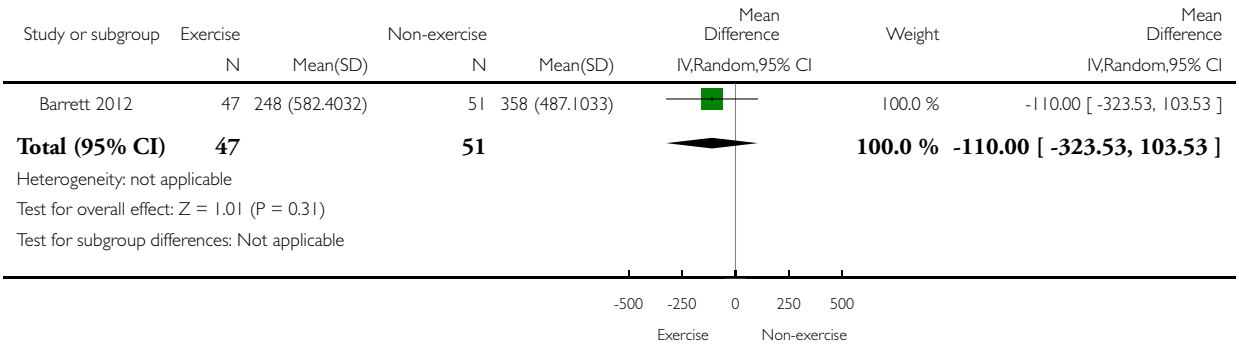
Test for subgroup differences: Not applicable

## Analysis 1.3. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 3 Severity of ARI.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 3 Severity of ARI



## Analysis 1.4. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 4 Number of symptom days in the follow-up period (12 weeks).

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 4 Number of symptom days in the follow-up period (12 weeks)

| Study or subgroup | Exercise N | Mean(SD) | Non-exercise N | Mean(SD) | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Barrett 2012 | 47 | 2.19 (4.99) | 51 | 3.65 (5.79) | | 51.7 % | -1.46 [ -3.60, 0.68 ] |
| Klentrou 2002 | 9 | 11 (8.8714) | 10 | 8.65 (7.7595) | | 8.7 % | 2.35 [ -5.18, 9.88 ] |
| Nieman 1997 | 43 | 5.6 (5.9) | 48 | 9.4 (7.6) | | 39.7 % | -3.80 [ -6.58, -1.02 ] |
| **Total (95% CI)** | **99** | | **109** | | | **100.0 %** | **-2.06 [ -4.39, 0.27 ]** |

Heterogeneity: $Tau^2 = 1.55$; $Chi^2 = 3.12$, df = 2 (P = 0.21); $I^2 = 36\%$

Test for overall effect: Z = 1.73 (P = 0.083)

Test for subgroup differences: Not applicable

## Analysis 1.5. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 5 Number of symptom days per episode.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

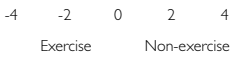
Outcome: 5 Number of symptom days per episode

| Study or subgroup | Exercise N | Mean(SD) | Non-exercise N | Mean(SD) | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Nieman 1990 | 18 | 3.6 (2.9698) | 18 | 7 (5.9397) | | 3.6 % | -3.40 [ -6.47, -0.33 ] |
| Barrett 2012 | 47 | 9.3 (5.13) | 51 | 11.4 (5.75) | | 7.1 % | -2.10 [ -4.25, 0.05 ] |
| Sloan 2013 | 16 | 5.3 (1.5) | 16 | 6.3 (2.2) | | 18.0 % | -1.00 [ -2.30, 0.30 ] |
| Ciloğ lu 2005 | 60 | 5.15 (1.5575) | 30 | 6.1 (1) | | 71.4 % | -0.95 [ -1.48, -0.42 ] |
| **Total (95% CI)** | **141** | | **115** | | | **100.0 %** | **-1.13 [ -1.71, -0.54 ]** |

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 3.30$, df = 3 (P = 0.35); $I^2 = 9\%$

Test for overall effect: Z = 3.78 (P = 0.00016)

Test for subgroup differences: Not applicable



## Analysis 1.6. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 6 Laboratory parameters - lymphocytes.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

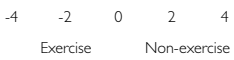
Outcome: 6 Laboratory parameters - lymphocytes

| Study or subgroup | Exercise N | Mean(SD) | Non-exercise N | Mean(SD) | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Nieman 1990 | 18 | 2.24 (0.6788) | 18 | 2.35 (0.5515) | | 23.2 % | -0.11 [ -0.51, 0.29 ] |
| Nieman 1993 | 14 | 2.6 (0.898) | 16 | 2.19 (0.68) | | 11.9 % | 0.41 [ -0.17, 0.99 ] |
| Nieman 1997 | 43 | 2.126 (0.5701) | 48 | 2 (0.4906) | | 64.9 % | 0.13 [ -0.09, 0.35 ] |
| **Total (95% CI)** | **75** | | **82** | | | **100.0 %** | **0.11 [ -0.10, 0.31 ]** |

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.21$, df = 2 (P = 0.33); $I^2 = 10\%$

Test for overall effect: Z = 1.04 (P = 0.30)

Test for subgroup differences: Not applicable

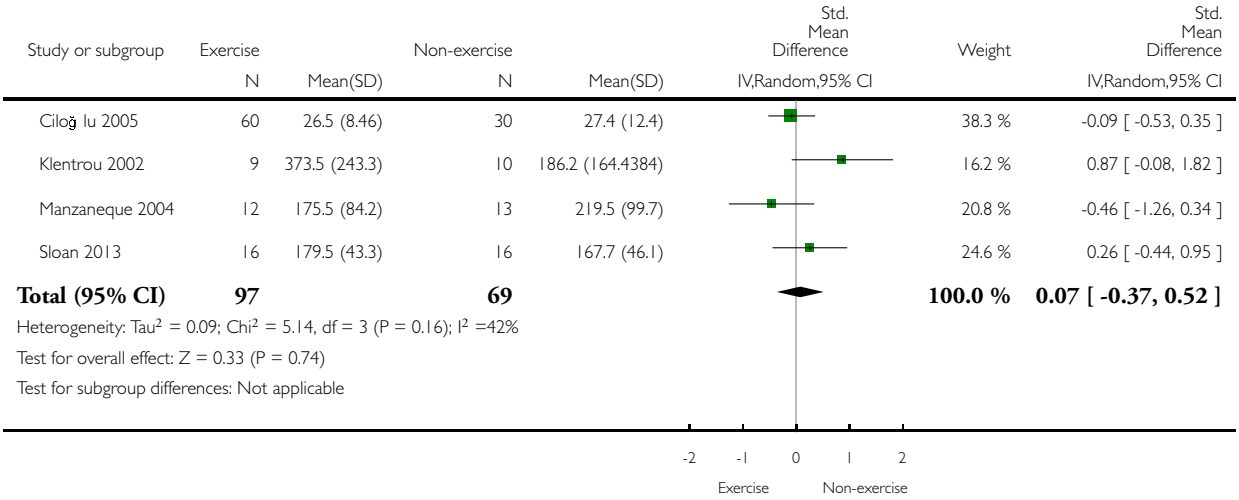


## Analysis 1.7. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 7 Laboratory parameters - IgA.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 7 Laboratory parameters - IgA



### Analysis 1.8. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 8 Laboratory parameters - neutrophils.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

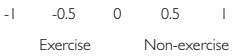
Outcome: 8 Laboratory parameters - neutrophils

| Study or subgroup | Exercise N | Mean(SD) | Non-exercise N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Barrett 2012 | 47 | 103.7 (512.2424) | 51 | 110.4 (311.1061) | | 43.9 % | -0.02 [ -0.41, 0.38 ] |
| Manzaneque 2004 | 12 | 2.85 (1.0254) | 13 | 3.63 (1.0254) | | 14.4 % | -0.74 [ -1.55, 0.08 ] |
| Nieman 1997 | 43 | 3.6 (1.0082) | 48 | 3.6 (1.0543) | | 41.8 % | 0.00 [ -0.41, 0.41 ] |
| **Total (95% CI)** | **102** | | **112** | | | **100.0 %** | **-0.11 [ -0.44, 0.22 ]** |

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 2.74$, df = 2 (P = 0.25); $I^2 = 27\%$

Test for overall effect: Z = 0.66 (P = 0.51)

Test for subgroup differences: Not applicable



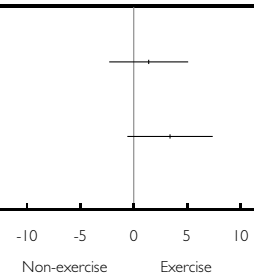

### Analysis 1.9. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 9 Quality of life.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 9 Quality of life

| Study or subgroup | Exercise N | Mean(SD) | Non-exercise N | Mean(SD) | Mean Difference IV,Random,95% CI | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|
| 1 Physical health | | | | | | |
| Barrett 2012 | 47 | 52 (8.8553) | 51 | 50.6 (9.9554) | | 1.40 [ -2.32, 5.12 ] |
| 2 Mental health | | | | | | |
| Barrett 2012 | 47 | 49.7 (10.2176) | 51 | 46.3 (9.9554) | | 3.40 [ -0.60, 7.40 ] |



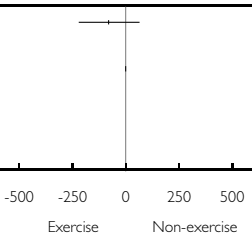
### Analysis 1.10. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 10 Cost to the patient (USD).

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 10 Cost to the patient (USD)

| Study or subgroup | Exercise N | Mean(SD) | Non-exercise N | Mean(SD) | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Barrett 2012 | 47 | 136 (293) | 51 | 214 (416) | | | -78.00 [ -219.60, 63.60 ] |
| **Subtotal (95% CI)** | **0** | | **0** | | | | **0.0 [ 0.0, 0.0 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 0.0 (P < 0.00001) | | | | | | | |



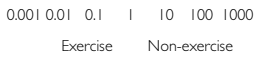
## Analysis 1.11. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 11 Exercise-related injuries.

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 11 Exercise-related injuries

| Study or subgroup | Exercise n/N | Non-exercise n/N | Risk Ratio M-H,Random,95% CI | Weight | Risk Ratio M-H,Random,95% CI |
|---|---|---|---|---|---|
| Nieman 1993 | 2/14 | 0/16 | | | 5.67 [ 0.29, 108.91 ] |
| **Subtotal (95% CI)** | **0** | **0** | | | **0.0 [ 0.0, 0.0 ]** |
| Total events: 2 (Exercise), 0 (Non-exercise) | | | | | |
| Heterogeneity: not applicable | | | | | |
| Test for overall effect: Z = 0.0 (P < 0.00001) | | | | | |

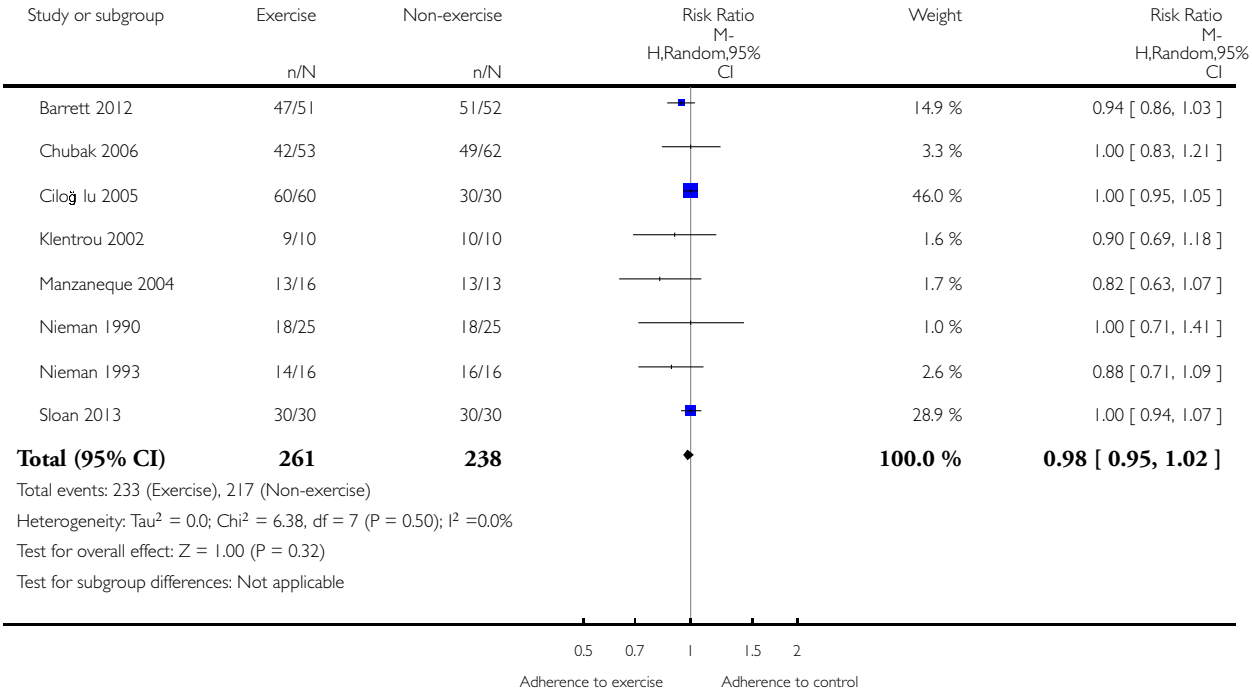


**Analysis 1.12. Comparison 1 Exercise versus control intervention for acute respiratory infections (total), Outcome 12 Adherence to the group intervention.**

Review: Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections

Comparison: 1 Exercise versus control intervention for acute respiratory infections (total)

Outcome: 12 Adherence to the group intervention




## ADDITIONAL TABLES

**Table 1. Characteristics of included studies - baseline**

| ID/location/full publication | n randomised/ withdrawals | % Female | Age | Information regarding participants |
|---|---|---|---|---|
| Manzaneque 2004/ Spain/yes | 29/3 | 51.7 | 18 to 21 years | Healthy, sedentary |
| Weidner 1998/USA/yes | 50/0 | 52 | 19 to 29 years | Moderately fit, maximal oxygen uptake value corresponding to > the 40th percentile for age and gender |
| Barrett 2012/USA/yes | 154/5 | 81,8 | 50 years or older | Healthy, sedentary |

**Table 1. Characteristics of included studies - baseline** (*Continued*)

| | | | | |
|---|---|---|---|---|
| Chubak 2006/USA/yes | 115/0 | 100 | 50 years or older | Overweight/obese, non-smoking, sedentary, post-menopausal women |
| Weidner 2003/USA/yes | 25/0 | 68.1 | 19 to 29 years | Sedentary |
| Nieman 1993/USA/yes | 32/2 | 100 | 67 to 85 years | Healthy, sedentary |
| Ciloğlu 2005/Turkey/yes | 90/0 | 100 | 45 to 65 years | Post-menopausal sedentary women |
| Klentrou 2002/Canada/yes | 20/0 | Not reported | 25 to 50 years | Sedentary men or women |
| Nieman 1990/USA/yes | 50/14 | 100 | 25 to 45 years | Mildly obese, sedentary women |
| Nieman 1997/USA/yes | 102/11 | 100 | 25 to 70 years | Obese, sedentary women |
| Sloan 2013/USA/yes | 32/0 | 100 | 54.1 ± 5.3 years | Healthy, post-menopausal women |

ID: study citation
USA: United States of America
ARI: acute respiratory infection

**Table 2. Characteristics of exercise interventions for ARI**

| ID/ location/ full publication | Type of exercise | Frequency | Intensity | Duration | Supervision | Comparison group | Outcomes in meta-analysis |
|---|---|---|---|---|---|---|---|
| Manzaneque 2004/Spain/yes | Qigong | 5 days per week | 8 distinct movements repeated 8 times to 30 minutes | 4 weeks | Qualified qigong instructor | Non-exercise | Adherence |
| Weidner 1998/USA/yes | Exercise | 6 days of exercise | 70% of HR reserve | 10 days | Supervised training | Non-exercise | Adherence; ARI symptoms |
| Barrett 2012/USA/yes | Bicycle, treadmill and brisk walk | One group contact (2.5 hours per week) + 45 minutes home practice per day | 12 to 16 Borg Scale | 8 weeks | Supervised by exercise physiologist | Meditation and non-exercise | Adherence; ARI episodes; ARI symptoms |

**Table 2. Characteristics of exercise interventions for ARI** *(Continued)*

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Chubak 2006/USA/yes | Bicycle, treadmill or walk | 5 days per week | 45 minutes of moderate-intensity exercise | 12 months | Supervised by exercise physiologist in the first 3 months | Once-weekly, 45-minute stretching sessions | Adherence; ARI episodes |
| Weidner 2003/USA/yes | Bicycle, walking or jogging | 5 days per week | 30 minutes at 70% of target heart rate | 7 days | Supervised | Non-exercise | Adherence |
| Nieman 1993/USA/yes | Brisk walking | 5 days per week | 30 to 40 minutes at 60% target heart rate | 12 weeks | Supervised | Callisthenics | Adherence; ARI episodes; lymphocytes |
| Ciloğ lu 2005/Turkey/yes | Walking on a treadmill or an outdoor tract | 5 days per week | 30 minutes each time respectively at 60% MHR | 12 weeks | Supervised | Outdoor exercise and non-exercise | Adherence; ARI symptoms |
| Klentrou 2002/Canada/yes | Bicycles, treadmills, stair climbers or combined | 3 days per week | 30 minutes at 75% HR reserve + 15 minutes stretching | 12 weeks | Supervised | Non-exercise | Adherence; ARI symptoms; salivary secretion immunoglobulin. |
| Nieman 1990/USA/yes | Walking | 5 days per week | 45 minutes at 60% reserve heart rate | 15 weeks | Supervised | Non-exercise | Adherence; ARI episodes; ARI symptoms; lymphocytes |
| Nieman 1997/USA/yes | Walking | 5 days per week | 45 minutes at 60% to 80% reserve heart rate | 12 weeks | Supervised | Non-exercise | Adherence; ARI symptoms; lymphocytes |
| Sloan 2013/USA/yes | Walking | 5 days per week | 30 minutes at 75% of individual HR max | 16 weeks | Not supervised | Non-exercise | ARI episodes; adherence; ARI symptoms; salivary secretion immunoglobulin |

ID: study citation
USA: United States of America
HR: heart rate
ARI: acute respiratory infection
NK: natural killer

# APPENDICES

## Appendix 1. MEDLINE (OVID)

1 respiratory tract infections/ or bronchitis/ or common cold/ or influenza, human/ or laryngitis/ or exp pharyngitis/ or exp pneumonia/ or exp sinusitis/
2 (respiratory adj2 (infect* or illness or symptom* or acute or virus*)).tw.
3 (common cold* or colds or coryza).tw.
4 ((acute or viral or virus* or bacter*) adj2 rhinit*).tw.
5 (influenza* or flu or ili).tw.
6 (pharyngit* or laryngit* or tonsillit* or sore thoat*).tw.
7 (throat* adj3 (infect* or inflam*)).tw.
8 (nasopharyngit* or rhinopharyngit*).tw.
9 Cough/
10 cough*.tw.
11 (sinusit* or rhinosinusit* or nasosinusit*).tw.
12 (bronchit* or pneumon* or bronchopneumon* or pleuropneumon*).tw.
13 (ari or urti or lrti).tw.
14 or/1-13
15 exp Exercise/
16 exp Exercise Movement Techniques/
17 exp Exercise Therapy/
18 Physical Fitness/
19 physical endurance/ or exercise tolerance/
20 Physical Exertion/
21 exp Sports/
22 Dancing/
23 (exercis* or sport* or fitness* or gym* or aerobic*).tw.
24 ((weight* or strength* or enduranc* or circuit*) adj5 (program* or train* or session*)).tw.
25 (physical* adj5 (fit* or activ* or movement* or train* or condition* or program*)).tw.
26 (activ* adj2 life*).tw.
27 (run* or walk* or jog* or sprint* or treadmill* or row* or swim* or bicycl* or cycl* or danc* or yoga or tai chi or tai ji or qigong or qi gong).tw.
28 or/15-27
29 14 and 28

## Appendix 2. EMBASE (Elsevier) search strategy

#37 #25 AND #36 27022
#36 #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 1390178
#35 run*:ab,ti OR walk*:ab,ti OR jog*:ab,ti OR sprint*:ab,ti OR treadmill*:ab,ti OR row*:ab,ti OR swim*:ab,ti OR bicycl*:ab,ti OR cycl*:ab,ti OR danc*:ab,ti OR yoga:ab,ti OR 'tai chi':ab,ti OR 'tai ji':ab,ti OR qigong:ab,ti OR 'qi gong':ab,ti AND [embase]/lim 976799
#34 (activ* NEAR/2 life*):ab,ti AND [embase]/lim 5574
#33 (physical* NEAR/5 (fit* OR activ* OR movement* OR train* OR condition* OR program*)):ab,ti AND [embase]/lim 74609
#32 ((weight* OR strength* OR enduranc* OR circuit*) NEAR/5 (program* OR train* OR session*)):ab,ti AND [embase]/lim 18505
#31 exercis*:ab,ti OR sport*:ab,ti OR fitness*:ab,ti OR gym*:ab,ti OR aerobic*:ab,ti AND [embase]/lim 267006
#30 'sport'/exp AND [embase]/lim 58241
#29 'training'/de OR 'endurance'/de OR 'exercise tolerance'/de OR 'physical capacity'/de AND [embase]/lim 78874
#28 'physical activity'/exp OR 'physical activity, capacity and performance'/de AND [embase]/lim166092
#27 'kinesiotherapy'/exp AND [embase]/lim 29817
#26 'exercise'/exp AND [embase]/lim 140065

#25 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 427944
#24 (throat* NEAR/3 (infect* OR inflam*)):ab,ti AND [embase]/lim 750
#23 cough*:ab,ti AND [embase]/lim 34249
#22 'coughing'/de AND [embase]/lim 46685
#21 influenza*:ab,ti OR 'flu'/de OR ili:ab,ti AND [embase]/lim 75233
#20 'influenza'/exp AND [embase]/lim 38070
#19 ((acute OR viral OR virus* OR bacter*) NEAR/2 rhinitis):ab,ti AND [embase]/lim 263
#18 'common cold':ab,ti OR 'common colds':ab,ti OR colds:ab,ti OR coryza:ab,ti AND [embase]/lim 3569
#17 'common cold'/de OR 'common cold symptom'/de AND [embase]/lim 4712
#16 sinusit*:ab,ti OR rhinosinusit*:ab,ti OR nasosinusit*:ab,ti AND [embase]/lim 13953
#15 'sinusitis'/exp AND [embase]/lim 21736
#14 nasopharyngit*:ab,ti OR rhinopharyngit*:ab,ti AND [embase]/lim 774
#13 pharyngit*:ab,ti OR laryngit*:ab,ti OR tonsillit*:ab,ti OR 'sore throat':ab,ti OR 'sore throats':ab,ti AND [embase]/lim 10891
#12 'sore throat'/de AND [embase]/lim 7948
#11 'tonsillitis'/exp AND [embase]/lim 7170
#10 'laryngitis'/de AND [embase]/lim 2091
#9 'pharyngitis'/exp AND [embase]/lim 15830
#8 bronchit*:ab,ti AND [embase]/lim 15281
#7 'bronchitis'/exp AND [embase]/lim 33544
#6 pneumon*:ab,ti OR bronchopneumon*:ab,ti OR pleuropneumon*:ab,ti AND [embase]/lim 124552
#5 'pneumonia'/exp AND [embase]/lim 141952
#4 'respiratory tract inflammation'/de OR 'inflammation of the lungs, bronchi and pleura'/de AND [embase]/lim 5088
#3 ari:ab,ti OR urti:ab,ti OR lrti:ab,ti AND [embase]/lim 2690
#2 (respiratory NEAR/2 (infect* OR illness OR symptom* OR acute OR virus*)):ab,ti AND [embase]/lim 70124
#1 'respiratory tract infection'/de OR 'upper respiratory tract infection'/de OR 'viral upper respiratory tract infection'/de OR 'lower respiratory tract infection'/de AND [embase]/lim 49071

## Appendix 3. CINAHL (EBSCO) search strategy

S38 S28 AND S37 398
S37 S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 181,452
S36 (MH "Quantitative Studies") 8,454
S35 TI placebo* OR AB placebo* 19,960
S34 (MH "Placebos") 6,623
S33 TI random* OR AB random* 99,149
S32 TI ((singl* or doubl* or tripl* or trebl*) W1 (blind* or mask*)) OR AB ((singl* or doubl* or tripl* or trebl*) W1 (blind* or mask*)) 14,511
S31 TI clinic* W1 trial* OR AB clinic* W1 trial* 27,568
S30 PT clinical trial 49,810
S29 (MH "Clinical Trials+") 112,137
S28 S14 AND S27 1,874
S27 S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 169,592
S26 TI (run* or walk* or jog* or sprint* or treadmill* or row* or swim* or bicycl* or cycl* or danc* or yoga or tai chi or tai ji or qigong or qi gong) OR AB (run* or walk* or jog* or sprint* or treadmill* or row* or
swim* or bicycl* or cycl* or danc* or yoga or tai chi or tai ji or qigong or qi gong) 60,655
S25 TI activ* N5 life* OR AB activ* N5 life* 4,190
S24 TI (physical* N5 (fit* or activ* or movement* or train* or condition* or program*)) OR AB (physical* N5 (fit* or activ* or movement* or train* or condition* or program*)) 24,749
S23 TI ( (weight* or strength* or enduranc* or circuit*) N5 (program* or train* or session*)) OR AB ((weight* or strength* or enduranc* or circuit*) N5 (program* or train* or session*)) 7,466
S22 TI (exercis* or sport* or fitness* or gym* or aerobic*) OR AB (exercis* or sport* or fitness* or gym* or aerobic*) 64,226

S21 (MH "Dancing+") 1,535
S20 (MH "Sports+") 33,190
S19 (MH "Exertion") OR (MH "Exercise Intensity") 8,146
S18 (MH "Physical Endurance+") 5,631
S17 (MH "Physical Fitness+") 7,255
S16 (MH "Therapeutic Exercise+") 25,339
S15 (MH "Exercise+") 47,369
S14 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 42,221
S13 TI (ari or urti or lrti) OR AB (ari or urti or lrti) 333
S12 TI (bronchit* or pneumon* or bronchopneumon* or pleuropneumon*) OR AB (bronchit* or pneumon* or bronchopneumon* or pleuropneumon*) 10,910
S11 TI (sinusit* or rhinosinusit* or nasosinusit*) OR AB (sinusit* or rhinosinusit* or nasosinusit*) 1,859
S10 TI cough* OR AB cough* 4,012
S9 (MH "Cough") 2,172
S8 TI (nasopharyngit* or rhinopharyngit*) OR AB (nasopharyngit* or rhinopharyngit*) 70
S7 TI (throat* N3 (infect* or inflam*)) OR AB (throat* N3 (infect* or inflam*)) 85
S6 TI (pharyngit* or laryngit* or tonsillit* or sore throat*) OR AB (pharyngit* or laryngit* or tonsillit* or sore thoat*) 728
S5 TI (influenza* or flu or ili) OR AB (influenza* or flu or ili) 10,739
S4 TI ((acute or viral or virus* or bacter*) N2 rhinit*) OR AB ((acute or viral or virus* or bacter*) N2 rhinit*) 30
S3 TI (common cold* or colds or coryza) OR AB (common cold* or colds or coryza) 888
S2 TI (respiratory N2 (infect* or illness or symptom* or acute or virus*)) OR AB (respiratory N2 (infect* or illness or symptom* or acute or virus*)) 8,217
S1 (MH "Respiratory Tract Infections") OR (MH "Bronchitis") OR (MH "Bronchitis, Acute") OR (MH "Common Cold") OR (MH "Influenza") OR (MH "Influenza, Human") OR (MH "Influenza, Seasonal") OR (MH "Laryngitis") OR (MH "Pharyngitis") OR (MH "Pneumonia+") OR (MH "Sinusitis+") OR (MH "Tonsillitis") 23,907

## Appendix 4. LILACS (Bireme) search strategy

**INGLS**

MH:"Respiratory Tract Infections" OR "Upper Respiratory Tract Infections" OR MH:C01.539.739$ OR MH:C08.730$ OR MH:Bronchitis OR MH:C08.127.446$ OR MH:C08.381.495.146 OR MH:C08.730.099 OR MH:"Common Cold" OR MH:C02.782.687.207$ OR MH:C08.730.162$ OR "Cold, Common" OR "Coryza, Acute" OR MH:"Influenza, Human" OR MH:C02.782.620.365$ OR MH:C08.730.310$ OR Grippe OR "Human Flu" OR "Human Influenza" OR "Influenza in Humans" OR MH:Laryngitis OR MH:C08.360.535 OR MH:C08.730.368 OR MH:C09.400.535 OR MH:Pharyngitis OR MH:C07.550.781$ OR MH:C08.730.561$ OR MH:C09.775.649$ OR "Sore Throat" OR MH:C08.381.677$ OR MH:08.730.610$ OR "Experimental Lung Inflammation" OR "Lobar Pneumonia" OR "Lung Inflammation" OR "Pulmonary Inflammation" OR MH:Sinusitis OR MH:C08.460.692.752$ OR MH:C08.730.749$ OR MH:C09.603.692.752$ OR MH:Nasopharyngitis OR MH:C07.550.350.700$ OR MH:C07.550.781.500$ OR MH:C08.730.561.500$ OR MH:C09.775.350.700$ OR MH:C09.775.649.500$ OR MH:Cough OR MH:Tos OR MH:Tosse OR MH:C08.618.248$ MH:C23.888.852.293$ OR MH:Bronchitis OR MH:Bronquitis OR MH:Bronquite OR MH:C08.127.446$ OR MH:C08.381.495.146$ OR MH:C08.730.099$ OR MH:Bronconeumonía OR MH:C08.127.509$ OR MH:C08.381.677.127$ OR MH:C08.730.610.127$ OR MH:Pleuropneumonia OR MH:C08.381.677.473$ OR MH:C08.528.735.473$ OR MH:C08.730.582.473$ OR MH:C08.730.610.473$ AND MH:Exercise OR "Aerobic Exercise" OR "Exercise, Aerobic" OR "Exercise, Isometric" OR "Exercise, Physical" OR "Isometric Exercise" OR MH:G11.427.590.530.698.277$ OR MH:I03.350$ OR MH:"Exercise Movement Techniques" OR MH:"Exercise Therapy" OR OR MH:E02.779.483$ OR MH:E02.831.387$ OR MH:"Physical Fitness" OR "Physical Conditioning, Human" OR MH:I03.621$ OR MH:N01.400.545$ OR MH:"Physical Endurance" OR MH:G11.427.680$ OR MH:I03.450.642.845.054.600$ OR MH:"Exercise Tolerance" OR MH:G11.427.680.270$ OR MH: "Physical Exertion" OR "Physical Effort" OR MH:G11.427.590.780$ OR MH:Sports OR Athletics OR MH:I03.450.642.845$ OR MH:Dancing OR MH:I03.450.642.287$ OR MH:Gymnastics OR Calisthenics OR MH:I02.233.543.454$ OR MH:I03.450.642.845.417$ OR MH:"Weight Lifting" OR MH:I03.450.642.845.950$ OR MH:"Muscle Strength" OR MH:E01.370.600.425$ OR MH:G11.427.560$ OR MH: "Physical Education and Training" OR MH:I02.233.543$ OR MH:Running OR MH:G11.427.590.530.568.610$ OR MH:G11.427.590.530.698.277.750$ OR MH:I03.450.642.845.610$ OR MH:Jogging OR MH:G11.427.590.530.568.610.320$ OR MH:G11.427.590.530.698.277.750.320$

OR MH:I03.450.642.845.610.320$ OR MH: "Exercise Test" OR Bicycle OR "Ergometry Test" OR "Arm Ergometry Test" OR "Step Test" OR "Stress Test" OR "Treadmill Test" OR MH:E01.370.370.380.250$ OR MH:E01.370.386.700.250$ OR MH: E05.333.250$ OR "Prueba Ergométrica de Bicicleta" OR "Test Ergométrico de Bicicleta" OR MH:Swimming OR Natación OR Natação OR MH:G11.427.590.530.568.800$ OR MH:G11.427.590.530.698.277.875$ OR MH:I03.450.642.845.869$ OR MH:Bicycling OR MH:I03.450.642.845.140$ OR MH:Yoga OR MH:E02.190.525.937$ OR MH:E02.190.901.984$ OR MH: E02.779.474.937$ OR MH:K01.844.799.867$ OR MH:"Tai Ji" OR MH:E02.190.525.890$ OR MH:E02.779.474.913$ OR MH: I03.450.642.845.560.500$ OR MH:"Breathing Exercises" OR "Ch'i Kung" OR "Qi Gong" OR Qigong OR "Respiratory Muscle Training" OR MH:E02.190.525.186$ OR MH:E02.779.474.124$ OR "Ch'i Kung" OR "Qi Gong" OR Qigong

**PORTUGUES**

MH:"Infecções Respiratórias" OR "Infecções das Vias Respiratórias" OR "Infecções do Trato Respiratório Superior" OR "Infecções do Aparelho Respiratório" OR "Infecções das Vias Respiratórias Superiores" OR "Infecções das Vias Aéreas Superiores" OR "Infecções do Sistema Respiratório" OR "Infecções do Sistema Respiratório Superior" OR "Infecções do Trato Respiratório" OR MH:Bronquitis OR MH: "Resfriado Comum" OR "Coriza Aguda" OR Catarro OR Resfriado OR Constipação OR MH: "Gripe Humana" OR MH:"Influenza Humana" OR Gripe OR "Gripe Humana" OR "Influenza em Humanos" OR MH:Laringite OR MH:Faringite OR Inflamação OR "Experimental dos Pulmões" OR "Inflamação do Pulmão" OR "Pneumonia Lobar" OR Pneumonite OR "Inflamação Pulmonar" OR Pulmonia OR MH:Sinusite OR MH:Nasofaringite OR MH:Bronchopneumonia OR MH:Pleuroneumonía AND MH:Exercício OR "Exercício Aeróbico" OR "Exercício Isométrico" OR "Exercício Físico" OR MH:"Terapia por Exercício" OR MH:"Aptidão Física" OR "Estado Físico Humano" OR "Condicionamento Físico Humano" OR MH:"Resistência Física" OR MH:"Tolerância ao Exercício" OR MH:"Esforço Físico" OR MH:Esportes OR Atletismo OR Desportes OR MH:Dança OR MH:Ginástica OR MH:"Levantamento de Peso" OR MH:"Força Muscular" OR "Educação Física e Treinamento" OR "Educação Física" OR "Educação e Treinamento Físico" OR MH:"Corrida Moderada" OR MH:Corrida OR MH:Trote OR MH:"Teste de Esforço" OR "Teste Ergométrico de Bicicleta" OR "Teste Ergométrico com os Braços" OR "Teste de Degrau" OR "Teste de Estresse" OR "Teste de Stress" OR "Teste de Esteira Rolante" OR "Teste Ergométrico de Esteira" OR MH:Ciclismo OR MH:Yoga OR "T'ai Chi" OR "Tai Chi" OR "Tai Ji Quan" OR "Tai-ji" OR Taiji OR Taijiquan OR MH:"Tai Ji" OR MH:"Ejercicios Respiratorios" OR "Qi Gong" OR Qigong OR "Exercícios para os Músculos Respiratórios" OR "Exercício Respiratório"

**ESPANHOL**

MH:"Infecciones del Sistema Respiratorio" OR "Infecciones de las Vías Respiratorias" OR "Infecciones del Tracto Respiratorio Superior" OR "Infecciones del Aparato Respiratorio" OR "Infecciones de las Vías Respiratorias Superiores" OR "Infecciones del Tracto Respiratorio" OR "Infecciones Respiratorias" OR MH:"Resfriado Común" OR "Coriza Aguda" OR Catarro OR Gripe "Influenza Humana" OR "Influenza en Humanos" OR MH:Laringitis OR MH:Faringitis OR "Dolor de Garganta" OR "Dor de Garganta" OR MH:Pneumonia OR MH:Neumonía OR MH:Pneumonia OR "Pneumonia, Lobar" OR Pneumonitis OR "Inflamación Experimental del Pulmón" OR "Inflamación del Pulmón" OR "Neumonía Lobar" OR Neumonitis OR "Inflamación Pulmonar" OR Pneumonía OR Pulmonía OR MH:Sinusitis OR MH:Nasofaringitis OR MH:Broncopneumonia OR MH:Pleuropneumonia AND MH:Ejercicio OR "Ejercicio Aeróbico" OR "Ejercicio Isométrico" OR "Ejercicio Físico" OR MH:"Técnicas de Ejercicio con Movimientos" OR MH: "Técnicas de Exercício e de Movimento" OR MH:E02.779.474$ OR "Técnicas de Ejercicios con Movimiento" OR "Técnicas por Movimiento de Ejercicio" OR "Técnicas de Movimentos do Exercício" OR MH:"Terapia por Ejercicio" OR MH: "Acondicionamiento Físico" OR MH:"Resistencia Física" OR MH:"Tolerancia al Ejercicio" OR MH:"Esfuerzo Físico" OR MH:Deportes OR Atletismo OR Desportos OR MH:Baile OR MH:Gimnasia OR Calistenia OR MH:"Levantamiento de Peso" OR MH:"Fuerza Muscular" OR MH: "Educación y Entrenamiento Físico" OR "Educación Física" OR MH:Carrera OR MH:"Prueba de Esfuerzo" OR "Test de Esfuerzo" OR "Prueba Ergométrica del Brazo" OR "Test Ergométrico del Brazo" OR "Prueba del Escalón" OR "Test del Escalón" OR "Prueba de Estrés" OR "Test de Estrés" OR "Prueba de Esfuerzo en Cinta sin Fin" OR MH:Ciclismo OR MH:Ioga OR MH:"Tai Ji" OR "T'ai Chi" OR "Tai Chi" OR "Tai Ji Quan" OR Tai-I OR Taiji OR Taijiquan OR MH:"Exercícios Respiratórios" OR "Entrenamiento del Musculo Respiratorio" OR "Ch'i Kung"

## Appendix 5. SPORTDiscus (EBSCO) search strategy

S40 S33 AND S39 101
S39 S34 OR S35 OR S36 OR S37 OR S38 OR S39 35,613
S38 TI ( crossover* or cross over* ) OR AB ( crossover* or cross over* ) 2,991
S37 TI ( (singl* or doubl*) W1 (blind* or mask*) ) OR AB ( (singl* or doubl*) W1 (blind* or mask*) ) 4,406
S36 TI trial 5,644
S35 TI clinic* W1 trial* OR AB clinic* W1 trial* 4,508
S34 TI placebo* OR AB placebo* 6,609
S33 TI random* OR AB random* 26,226
S32 S19 AND S31 3,150
S31 S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 713,457
S30 TI ( run* or walk* or jog* or sprint* or treadmill* or row* or swim* or bicycl* or cycl* or danc* or yoga or tai chi or tai ji or qigong or qi gong ) OR AB ( run* or walk* or jog* or sprint* or treadmill* or row* or
swim* or bicycl* or cycl* or danc* or yoga or tai chi or tai ji or qigong or qi gong ) 216,308
S39 TI activ* N2 life* OR AB activ* N2 life* 2,393
S28 TI ( physical* N5 (fit* or activ* or movement* or train* or condition* or program*) ) OR AB ( physical* N5 (fit* or activ* or movement* or train* or condition* or program*) ) 49,909
S27 TI ( (weight* or strength* or enduranc* or circuit*) N5 (program* or train* or session*) ) OR AB ( (weight* or strength* or enduranc* or circuit*) N5 (program* or train* or session*) ) 22,558
S26 TI ( exercis* or sport* or fitness* or gym* or aerobic* ) OR AB ( exercis* or sport* or fitness* or gym* or aerobic* ) 370,918
S25 DE "DANCE" OR DE "AERIAL dance" OR DE "AEROBIC dancing" OR DE "AFRICAN American dance" OR DE "BALLET" OR DE "BALLROOM dancing" OR DE "BELLY dance" OR DE "BREAK dancing" OR DE "CHA-cha (Dance)" OR DE "COUNTRY dancing" OR DE "DANCE for people with disabilities" OR DE "FLAMENCO" OR DE "FOLK dancing" OR DE "FREE skating" OR DE "HIP-hop dance" OR DE "ICE
dancing" OR DE "JAZZ dance" OR DE "LINE dancing" OR DE "LION dance" OR DE "MODERN dance" OR DE "MOVEMENT notation" OR DE "ORIGINAL set pattern dance (Skating)" OR DE "POLE dancing" OR DE "ROUND dancing" OR DE "SALSA (Dance)" OR DE "SHISHIMAI (Dance)" OR DE "SQUARE dancing" OR DE "STEP dancing" OR DE "TANGO (Dance)" OR DE "TAP dancing" 7,883
S24 DE "PHYSICAL training & conditioning" OR DE "ACROBATICS -- Training" OR DE "ALTITUDE training" OR DE "ANAEROBIC training" OR DE "ARCHERY -- Training" OR DE "BADMINTON (Game) -- Training" OR DE "BASE training (Exercise)" OR DE "BASEBALL -- Training" OR DE "BASKETBALL -- Training" OR DE "BICYCLE racing -- Training" OR DE "BODYBUILDING -- Training" OR DE
"BOWLING -- Training" OR DE "BOXING -- Training" OR DE "BULLFIGHT training & conditioning" OR DE "BUNGEE jumping training & conditioning" OR DE "CANOES & canoeing -- Training" OR DE "CAVING training & conditioning" OR DE "COMPOUND exercises" OR DE "CONTRAST training (Physical training & conditioning)" OR DE "COXSWAINING -- Training" OR DE "CRICKET training &
conditioning" OR DE "CROSS-training (Sports)" OR DE "CYCLING -- Training" OR DE "DANCE training & conditioning" OR DE "DEEP diving training & conditioning" OR DE "DIVING -- Training" OR DE "DOGSLEDDING training & conditioning" OR DE "ENDURANCE sports -- Training" OR DE "FENCING -- Training" OR DE "FIELD hockey training & conditioning" OR DE "FOOTBALL -- Training" OR DE "FUNCTIONAL training" OR DE "GLIDING & soaring training & conditioning" OR DE "GOLF -- Training" OR DE "GYMNASTICS -- Training" OR DE "HANDBALL training & conditioning" OR DE "HIKING training & conditioning" OR DE "HOCKEY -- Training" OR DE "HUNTING training & conditioning" OR DE "INTERVAL training" OR DE "ISOLATION exercises" OR DE "KAYAKING -- Training" OR DE "KNIFE fighting -- Training" OR DE "KORFBALL -- Training" OR DE "LACROSSE training & conditioning" OR DE "LONG slow distance training" OR DE "MARTIAL arts -- Training" OR DE "MOTORSPORTS training & conditioning" OR DE "MOUNTAINEERING -- Training" OR DE "NUNCHAKU -- Training" OR DE "ORIENTEERING -- Training" OR DE "OVERTRAINING" OR DE "PACE training" OR DE "PARACHUTING training & conditioning" OR DE "PARAKITING training & conditioning" OR DE "PERIODIZATION training" OR DE "PERSONAL training" OR DE "POLO training & conditioning" OR DE "PRACTICE (Sports)" OR DE "PRESEASON (Sports)" OR DE "RACQUETBALL -- Training" OR DE "RECOVERY training" OR DE "RELAY racing -- Training" OR DE "REPETITION training" OR DE "RESISTANCE training (Physical
training & conditioning)" OR DE "ROCK climbing -- Training" OR DE "RODEO training & conditioning" OR DE "ROLLER skating training & conditioning" OR DE "ROWING -- Training" OR DE "RUGBY football -- Training" OR DE "RUNNING -

- Training" OR DE "SHOT putting -- Training" OR DE "SKATING -- Training" OR DE "SKIS & skiing -- Training" OR DE "SKYDIVING training & conditioning" OR DE "SOCCER -- Training" OR DE "SOFTBALL -- Training" OR DE "SPEED endurance training" OR DE "SQUASH (Game) -- Training" OR DE "STRENGTH training" OR DE "SURFING -- Training" OR DE "SWIMMING --
Training" OR DE "TABLE tennis training & conditioning" OR DE "TEAM handball -- Training" OR DE "TENNIS -- Training" OR DE "TRACK & field -- Training" OR DE "TRIATHLON -- Training" OR DE "TUG of war (Game) -- Training" OR DE "VAULTING (Horsemanship) -- Training" OR DE "VOLLEYBALL -- Training" OR DE "WATER polo -- Training" OR DE "WEIGHT training" OR DE "WHEELCHAIR sports -- Training" OR DE "WINTER sports training & conditioning" OR DE "WRESTLING -- Training" OR DE "YOGA training & conditioning" 38,599
S23 DE "BALL games" OR DE "ANETSO" OR DE "BALL hockey" OR DE "BALLE au tamis (Game)" OR DE "BASEBALL" OR DE "BASKETBALL" OR DE "BATTLE ball" OR DE "BICYCLE polo" OR DE "BILLIARDS" OR DE "BOWLING games" OR DE "BROOMBALL" OR DE "CAMOGIE (Game)" OR DE "CRICKET (Sport)" OR DE "CROQUET" OR DE "DODGEBALL" OR DE "FIELD hockey" OR DE "FLICKERBALL" OR DE "FOOTBALL" OR DE "GOAL ball" OR DE "GOLF" OR DE "GOLF croquet" OR DE "HANDBALL" OR DE "HURLING (Game)" OR DE "INDOOR hockey" OR DE "JAPANESE
polo" OR DE "JIAN zi (Game)" OR DE "KANG (Game)" OR DE "KICKBALL" OR DE "LACROSSE" OR DE "LAPTA (Game)" OR DE "LAWN tempest (Game)" OR DE "MINTON (Game)" OR DE "PARLOR football" OR DE "PARLOR tennis" OR DE "PICKLE ball" OR DE "PICKLEBALL (Game)" OR DE "PIZE-ball" OR DE "POLO" OR DE "POLOCROSSE" OR DE "PUSH ball" OR DE "QUIDDITCH (Game)" OR DE "RACQUETBALL" OR DE "RAGA (Game)" OR DE "ROLL ball" OR DE "ROUNDERS" OR DE "RUGBALL" OR DE "SCHLAGBALL" OR DE "SHINTY (Game)" OR DE "SOCCER" OR DE "SOFTBALL" OR DE "SPEED-a-way (Game)" OR DE "SPEEDBALL" OR DE "STICKBALL (Game)" OR DE "STOOLBALL" OR DE "TABLE tennis" OR DE "TCHOUKBALL" OR DE "TENNIS" OR DE "TETHERBALL" OR DE "TRAPBALL" OR DE "VOLLEYBALL" OR DE "WALLYBALL" OR DE "WATER polo" OR DE "WICKET" OR DE "WIFFLE ball" 108,135
S22 DE "EXERCISE tolerance" 12
S21 DE "PHYSICAL fitness" OR DE "ANAEROBIC exercises" OR DE "ASTROLOGY & physical fitness" OR DE "BODYBUILDING" OR DE "CARDIOVASCULAR fitness" OR DE "CIRCUIT training" OR DE "COMPOUND exercises" OR DE "ISOLATION exercises" OR DE "LIANGONG" OR DE "MUSCLE strength" OR DE "PERIODIZATION training" OR DE "PHYSICAL fitness -- Genetic aspects" OR DE "PHYSICAL
fitness for children" OR DE "PHYSICAL fitness for girls" OR DE "PHYSICAL fitness for men" OR DE "PHYSICAL fitness for older people" OR DE "PHYSICAL fitness for people with disabilities" OR DE "PHYSICAL fitness for women" OR DE "PHYSICAL fitness for youth" OR DE "SPORT for All" 96,632
S20 DE "EXERCISE" OR DE "ABDOMINAL exercises" OR DE "AEROBIC exercises" OR DE "ANAEROBIC exercises" OR DE "AQUATIC exercises" OR DE "ARM exercises" OR DE "BACK exercises" OR DE "BREATHING exercises" OR DE "BREEMA" OR DE "BUTTOCKS exercises" OR DE "CALISTHENICS" OR DE "CHAIR exercises" OR DE "CHEST exercises" OR DE "CIRCUIT training" OR DE "COMPOUND exercises" OR DE "DO-in" OR DE "EXERCISE -- Immunological aspects" OR DE "EXERCISE adherence" OR DE "EXERCISE for children" OR DE "EXERCISE for girls" OR DE
"EXERCISE for men" OR DE "EXERCISE for middle-aged persons" OR DE "EXERCISE for older people" OR DE "EXERCISE for people with disabilities" OR DE "EXERCISE for women" OR DE "EXERCISE for youth" OR DE "EXERCISE therapy" OR DE "EXERCISE video games" OR DE "FACIAL exercises" OR DE "FALUN gong exercises" OR DE "FOOT exercises" OR DE "GYMNASTICS" OR DE "HAND exercises" OR DE "HATHA yoga" OR DE "HIP exercises" OR DE "ISOKINETIC exercise" OR DE "ISOLATION exercises" OR DE "ISOMETRIC exercise" OR DE "ISOTONIC exercise" OR DE "KNEE exercises" OR DE "LEG
exercises" OR DE "LIANGONG" OR DE "METABOLIC equivalent" OR DE "MULAN quan" OR DE "MUSCLE strength" OR DE "PILATES method" OR DE "PLYOMETRICS" OR DE "QI gong" OR DE "REDUCING exercises" OR DE "RUNNING" OR DE "RUNNING -- Social aspects" OR DE "SCHOOLS -- Exercises & recreations" OR DE "SEXUAL exercises" OR DE "SHOULDER exercises" OR DE "STRENGTH training" OR DE "STRESS management exercises" OR DE "STRETCHING exercises" OR DE "TAI chi" OR DE "TREADMILL exercise" OR DE "WHEELCHAIR workouts" OR DE "YOGA" 136,880
S19 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 9,462
S18 TI ( ari or urti or lrti ) OR AB ( ari or urti or lrti ) 246
S17 TI ( bronchit* or pneumon* or bronchopneumon* or pleuropneumon* ) OR AB ( bronchit* or pneumon* or bronchopneumon* or pleuropneumon* ) 685
S16 TI ( sinusit* or rhinosinusit* or nasosinusit* ) OR AB ( sinusit* or rhinosinusit* or nasosinusit* ) 129
S15 TI cough* OR AB cough* 839

S14 TI ( nasopharyngit* or rhinopharyngit* ) OR AB ( nasopharyngit* or rhinopharyngit* ) 10
S13 TI ( throat* N3 (infect* or inflam*) ) OR AB ( throat* N3 (infect* or inflam*) ) 18
S12 TI ( pharyngit* or laryngit* or tonsillit* or sore throat* ) OR AB ( pharyngit* or laryngit* or tonsillit* or sore thoat* ) 48
S11 TI ( influenza* or flu or ili ) OR AB ( influenza* or flu or ili )1,179
S10 TI ( (acute or viral or virus* or bacter*) N2 rhinit* ) OR AB ( (acute or viral or virus* or bacter*) N2 rhinit* ) 3
S9 TI ( common cold* or colds or coryza ) OR AB ( common cold* or colds or coryza ) 5,846
S8 TI ( respiratory N2 (infect* or illness or symptom* or acute or virus*) ) OR AB ( respiratory N2 (infect* or illness or symptom* or acute or virus*) ) 936
S7 DE "BRONCHITIS" 83
S6 DE "COUGH" 148
S5 DE "PNEUMONIA" 176
S4 DE "SINUSITIS" 114
S3 DE "INFLUENZA" 378
S2 DE "COLD (Disease)" 419
S1 DE "RESPIRATORY infections" 457

## CONTRIBUTIONS OF AUTHORS

AJG co-ordinated the retrieval of papers and wrote the background, methods, results, discussion and conclusion. JK participated in the retrieval of papers and co-wrote the background, methods, results, discussion and conclusion. TH co-wrote the background, methods, results, discussion and conclusion. CDM co-wrote the background, methods, results, discussion and conclusion. EB helped with data analysis and co-wrote the methods, results and discussion.

## DECLARATIONS OF INTEREST

Antonio Jose Grande: none known.

Justin Keogh: none known.

Tammy Hoffmann: none known.

Elaine M Beller: this review was supported in part by an Australia Fellowship Grant from the NHMRC, Australia, to the Centre for Evidence Based Practice, Bond University.

Chris B Del Mar: none known.

## SOURCES OF SUPPORT

### Internal sources

- None, Other.

### External sources

- None, Other.

## DIFFERENCES BETWEEN PROTOCOL AND REVIEW

One quasi-RCT (not specifically excluded in our protocol) was found in the search (Weidner 2003). We included it in the review, although it contributed no data to the meta-analysis.

We changed the title of the review from 'Exercise for acute respiratory infections' to 'Exercise versus no exercise for the occurrence, severity and duration of acute respiratory infections' to more accurately describe the focus of the review.

We included *"The proportion of people who experienced at least one ARI over the study period"* as a primary outcome even though it was not nominated in the protocol, because we judged this outcome to be important to the understanding of ARI episodes. Similarly, we separated the outcome *"mean number of ARI symptoms days"* (not extractable from most trials) into two new outcomes (*"number of symptom days in the follow-up period"* and *"number of symptom days per episode"*), and included them as primary outcomes.

We had planned to compare exercise with no exercise, usual care, placebo and non-pharmacological treatments, but there were only data for exercise versus no exercise. We had also planned to calculate a number needed to treat to benefit (NNTB), but there were no significant dichotomous outcomes (only one continuous outcome was significant).

Had cross-over RCTs been included, we would only have included the phase before crossing over interventions; however, there were none. Similarly, had cluster-RCTs been included, we would have made statistical adjustments for clustering of participants; however, there were none.

We planned the following subgroup analyses: patient age; setting of the exercise; whether the exercise was supervised or not; any associated chronic conditions (asthma, diabetes, hypertension, chronic obstructive pulmonary disease); types of exercise (resistance, endurance, stretching); frequency of exercise (how many sessions/week); and intensity of exercise: light (1.6 to 2.9 metabolic equivalents (METs)), moderate (3 to 5.9 METs), vigorous ($\geq$ 6 METs). However, we only had data for length of the intervention, which we had not planned.

## INDEX TERMS

### Medical Subject Headings (MeSH)

*Exercise; Acute Disease; Bicycling; Randomized Controlled Trials as Topic; Respiratory Tract Infections [epidemiology; *prevention & control]; Time Factors; Walking

### MeSH check words

Female; Humans; Male